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CONTENTS

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STUDIES IN PREMATURITY. PART 4

DEVELOPMENT AND PROGRESS OF THE PREMATURELY BORN CHILD IN THE PRE-SCHOOL PERIOD

BY

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The previous papers in this series (Drillien, 1947) contain a detailed analysis and discussion of the etiology of prematurity, stillbirth, and infant death occurring in the Simpson Memorial Pavilion, Edinburgh, during the years 1943 to 1945 inclusive, a random 1 in 10 sample of full-term surviving infants born during the same period serving as a control. The present paper deals with the progress of the surviving premature infants included in the population studied. The first section gives a comparison of the medical history of premature and full-term babies before discharge from hospital, and the second section an account of a follow-up examination of a sample of the premature infants, now aged between one-and-a-half and four-and-a-half years, and of a control group of full-term children.

Section 1: Progress in Hospital

Infection rates in premature and mature infants. During the period under review the minimum length of stay in hospital for normal mothers and infants was ten days. Premature infants usually remained in hospital for much longer, but in order to compare infection rates in infants of different birth weights, only those cases of infection occurring within ten days of birth have been included. Infections occurring in infants who subsequently died in hospital have been dealt with in Part 3 (Drillien, 1947) and are not considered here. Twins have been excluded. Data were obtained from paediatric records of all the surviving premature infants, and one in ten of the surviving full-term infants.

The infections recorded were: (1) thrush; (2) septic skin infections, mainly staphylococcal; (3) discharging eyes, excluding those cases resulting from instillation of silver nitrate solution; and (4) diarrhoea, with or without vomiting, excluding those cases considered to be due solely to dietary disturbance.

Table 1 gives the percentage of infants contracting one or more of the above infections during the first ten days of life. It will be seen that in the smallest weight group nearly one in three of those who survived contracted a minor infection, compared with one in sixteen of the mature infants. The infection rate falls steadily with increasing birth weight in the premature group, but after a birth weight of 5·5 lb. has been reached the infection rate remains steady at about 6 per cent. These differences between weight groups are highly significant, the chi-squared value being 31·20.

Table 2 gives the morbidity rate for each of the four infections mentioned according to birth weight. This shows that though the smallest infants have a much higher incidence of all infections except gastro-enteritis, birth weight when it is over 3·5 lb. does not appear to have a marked effect on infection rate except for thrush. This is demonstrated in fig. 1, where the average morbidity rate for each infection is taken to be 100, and the variations from this mean have been calculated for each weight group.

The higher incidence of thrush among premature infants is probably accounted for by the greater proportion of bottle-fed infants. Henderson (1943) in an investigation into the incidence of thrush in the Simpson Memorial Pavilion, found no striking difference between the incidence of thrush in bottle-fed infants, whether premature or mature.

It does seem, however, that the very smallest infants are particularly susceptible to septic infections, as shown by the high incidence of septic skin infections and discharging eyes. No cases of gastro-enteritis occurred in the smallest group in the first ten days, and very few cases in the 3·5 to 4·5 lb. group, though the largest premature infants had a much higher rate than the mature babies.

TABLE 1
MINOR INFECTIONS OCCURRING WITHIN THE FIRST TEN DAYS OF LIFE

Birth weight	No. of infants	Per cent. infected
2 lb. 9 oz. to 3 lb. 8 oz. ..	29	31·0
3 lb. 9 oz. to 4 lb. 8 oz. ..	124	13·7
4 lb. 9 oz. to 5 lb. 8 oz. ..	277	9·8
5 lb. 9 oz. to 10 lb. ..	576	6·0

* During the tenure of a Streatfield Research Scholarship of the Royal College of Physicians of London and the Royal College of Surgeons of England.

TABLE 2

SPECIFIC INFECTIONS OCCURRING WITHIN THE FIRST TEN DAYS OF LIFE

Birth weight	Incidence of cases of:			
	Thrush	Septic skin infection	Conjunctivitis	Gastro-enteritis
2 lb. 9 oz. to 3 lb. 8 oz.	17·2	13·8	6·9	—
3 lb. 9 oz. to 4 lb. 8 oz.	6·5	4·8	0·8	1·6
4 lb. 9 oz. to 5 lb. 8 oz.	2·9	2·5	1·8	3·3
5 lb. 9 oz. to 10 lb. 0 oz.	1·9	3·8	1·2	0·5
Average incidence in total sample ..	2·8	3·5	1·3	1·2

It seems reasonable to assume from this that smaller infants are more susceptible to gastro-enteritis if they come into contact with the infection. Infants under 4·5 lb. would almost certainly have been isolated in an incubator room for the first ten days, under ideal nursing conditions, whereas those over 4·5 lb. whose general condition was good would probably have been nursed alongside the mature infants in the main nursery.

Pathological conditions other than infections, occurring in the first ten days of life. Other pathological conditions occurring within the first few days of life were: (1) cyanotic attacks; (2) severe jaundice with oedema; (3) haemorrhagic disease; (4) cerebral signs, such as anxiety and restlessness and localized twitching or generalized convulsion, with or without respiratory and cardiac symptoms; and (5) dehydration fever, that is, a rise of temperature to 100° F., with loss of weight, there being no obvious signs of infection or other abnormality present. Again only infants surviving their discharge have been included. Table 3 gives the incidence of these conditions in premature and mature infants.

Section 2: Progress in Early Childhood

In order to trace the subsequent history of infants included in the survey, a follow-up clinic was held in 1947. Every married mother of a surviving infant who gave an Edinburgh address was written to and asked to attend this special clinic. Altogether 430 full-term and 285 premature infants were written for. The response was about 40 per cent. in each case. It was decided after the conclusion of the follow-up not to include the twins, about thirty in all, as their number was not large enough to constitute a separate group. The following sections are based on the history and examination of 277 children, 103 of them prematurely born, and 174 full-term children.

It is unlikely that this sample is a random one, there being two obvious sources of bias. First, those children whose progress was not satisfactory would be the more likely to attend, and secondly the more conscientious mothers would tend to bring their children back. But as the main purpose of the enquiry is a comparison between two groups, in both of which these sources of bias would operate, and as there is no attempt to draw conclusions applicable to the general population, the bias can be ignored.

A more serious source of error occurs because it was impossible to determine how many children had died after discharge from hospital. The Edinburgh Corporation Maternity and Child Welfare Department keeps a record of all deaths under one year of age occurring in the city, and the names of all children written for were checked against this record. In addition a number of mothers wrote to say that their children had died.

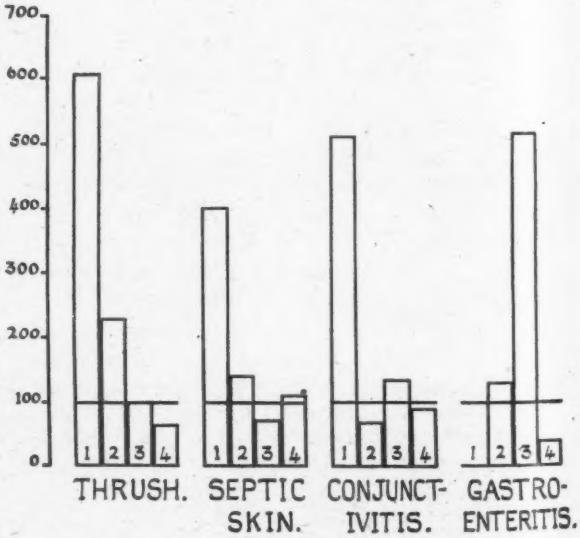

FIG. 1.—Relative infection rates in the first ten days of life, according to weight at birth; average rate of each infection being taken as 100.

Birth weight groups: (1) 2 lb. 9 oz. to 3 lb. 8 oz.; (2) 3 lb. 9 oz. to 4 lb. 8 oz.; (3) 4 lb. 9 oz. to 5 lb. 8 oz.; (4) 5 lb. 9 oz. to 10 lb.

TABLE 3

OTHER PATHOLOGICAL CONDITIONS OCCURRING WITHIN THE FIRST TEN DAYS OF LIFE

Birth weight	Incidence of cases of:				
	Cyanotic attacks	Cerebral signs	Jaundice	Haemorrhagic disease	Dehydration fever
4 lb. 8 oz. and under	9·8	—	2·0	2·0	—
4 lb. 9 oz. to 5 lb. 8 oz.	3·3	2·2	1·4	0·7	—
5 lb. 9 oz. and over	0·2	3·3	—	—	1·7

The number of deaths ascertained was seventeen out of the premature group (6 per cent. of those written for), and seven of the full-term group (1·6 per cent.). Although the figures are incomplete, it is certain that the number of deaths of prematurely born children surviving their discharge from hospital greatly exceeds that of full-term children.

Table 4 gives the age composition of the children attending the clinic.

A full history was taken from the mother as to the following: (1) method of feeding, from birth to weaning; (2) administration of vitamin supplements; (3) attendance at welfare clinics; (4) diphtheria immunization; (5) age at which the child sat, stood, walked, and talked; (6) infections, and other illnesses or abnormalities suffered by the child; (7) behaviour disorders; (8) housing conditions. A physical examination was also made.

Method of feeding. The following questions were put to each mother at the interview: (1) For how long did total and partial breast feeding continue? (2) In cases of failure to breast feed, to what cause did she attribute the failure? (3) In changing from breast to bottle feeding, what was the artificial food chosen, and on whose advice?

Infants were classified into five groups: those who were (1) never totally breast-fed, including cases where breast feeding continued for less than one week; (2) fully breast-fed for longer than one week but less than one month; (3) fully breast-fed longer than one, but less than three months; (4) fully breast-fed for longer than three months, but transferred wholly on to the bottle before the institution of mixed feeding; (5) fully breast-fed until weaning on to solid food, including those who after mixed feeding was started were taken off the breast, and given one, or at the most two bottles daily.

It will be seen from table 5 and fig. 2 that success in breast feeding depends largely on the birth weight of the infant. In over three-quarters of the smallest premature infants breast feeding was never attempted, while in the mature group nearly half the mothers fed their babies for longer than three months.

BREAST FEEDING IN PRIMIPARAE AND MULTIPARAE. Figs. 3 and 4 demonstrate the duration of breast feeding in primiparae and multiparae. With both premature and mature infants multiparae are more successful in breast feeding.

In the case of premature births an equal proportion of primiparae and multiparae begin by breast feeding, but the proportion of the former who continue to do so after discharge from hospital falls steadily below that of the multiparae. With mature infants the multiparae show a higher percentage of successful nursing right from the beginning. This is in spite of the fact that there will be a larger number of healthy mothers of first babies, multiparae only being admitted in event of some complication of pregnancy or delivery, or for social reasons.

CAUSES OF FAILURE TO BREAST FEED. The following reasons were given by mothers for failure in nursing: (1) insufficient lactation (the mother stated that the baby was dissatisfied, hungry, and failed to gain weight); (2) illness of the mother herself (either her condition after delivery was so poor that nursing was not allowed, or else after a successful period of breast feeding she became ill and feeding had to be abandoned); (3) prematurity of the baby (the baby was too small to be allowed to suck at the breast, and it proved impossible to keep up the milk supply by expression); (4) difficulty in getting the

TABLE 4

AGE COMPOSITION OF PREMATURE AND MATURE CHILDREN ATTENDING FOLLOW-UP CLINIC

	No. of children	
	Premature	Mature
1 yr. 6 mos. and under ..	—	7
1 yr. 7 mos. to 2 yrs. ..	11	26
2 yrs. 1 mo. to 2 yrs. 6 mos.	22	19
2 yrs. 7 mos. to 3 yrs. ..	20	44
3 yrs. 1 mo. to 3 yrs. 6 mos.	8	26
3 yrs. 7 mos. to 4 yrs. ..	15	37
4 yrs. 1 mo. to 4 yrs. 6 mos.	25	14
4 yrs. 7 mos. and over ..	2	1
Total	103	174

baby to fix (these infants were all premature but lusty enough to be put to the breast); (5) breast abscess; (6) retracted nipples; (7) other reasons.

Table 6 gives the causes of failure to breast feed premature and mature infants. In both groups insufficient lactation was the commonest cause. Breast abscess occurred much more commonly in the mature group.

TABLE 5

DURATION OF BREAST FEEDING ACCORDING TO BIRTH WEIGHT OF INFANT

Duration of breast feeding	Birth weight		
	4 lb. 8 oz. and under	4 lb. 9 oz. to 5 lb. 8 oz.	5 lb. 9 oz. and over
Never	76·0	35·9	14·4
Less than 1 month	4·0	12·8	18·4
Less than 3 months ..	8·0	9·0	18·4
3 months—weaning	——	12·8	10·3
Fully breast-fed	12·0	20·5	38·5
Total ..	100·0	100·0	100·0
No. of cases ..	25	78	174

Fig. 5 demonstrates at what stage in feeding these difficulties arise. In the premature group failure to attempt nursing was due to the prematurity of the infant in about 60 per cent. of the failures. Once feeding had been successfully established, the commonest cause of subsequent failure was insufficient lactation, this being the commonest cause of failure at every stage in the mature group.

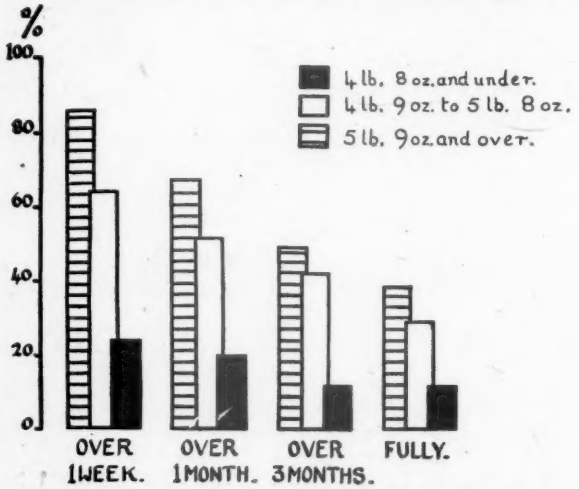

FIG. 2.—Duration of breast feeding according to birth weight.

In the British Paediatric Association survey of breast feeding in Birmingham (Neale and others, 1943), causes of failure were given as follows: anxiety of mother re progress of infant, 33 per cent.; illness of mother, 23 per cent.; mother returning to work, 15 per cent.; other reasons, 29 per cent.

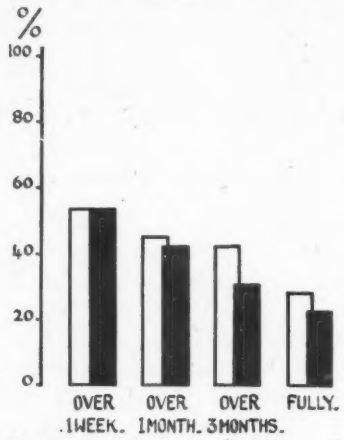

FIG. 3.—Duration of breast feeding of premature infants by primiparae and multiparae.
Outlined rectangles, multiparae.
Black ,, , primiparae.

ARTIFICIAL FEEDING. The artificial foods chosen as a substitute for breast feeding were classified as follows: (1) fresh milk; (2) national dried milk; (3) a proprietary dried milk preparation; (4) additions to fresh or dried milk, other than sugar, vitamin supplements, Virol, or mineral salts. The commonest addition was Sister Laura's food; others were Benger's food, oat flour, patent barley, and groats.

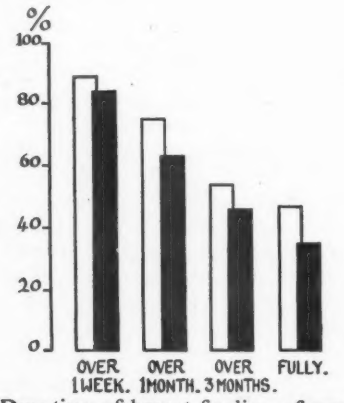

FIG. 4.—Duration of breast feeding of mature infants by primiparae and multiparae.
Outlined rectangles, multiparae.
Black ,, , primiparae.

Where several artificial foods had been tried, that one which had been used for the longest period was chosen for classification. The mother was asked on whose advice she gave the artificial food of choice. Where advice was given by doctor, clinic

TABLE 6

CAUSES OF FAILURE OF BREAST FEEDING IN PREMATURE AND MATURE INFANTS

Cause of failure	Per cent. of total infants		Per cent. of total failures	
	Premature	Mature	Premature	Mature
Insufficient lactation	29·1	36·2	39·0	58·9
Illness of mother	8·7	10·3	11·7	16·8
Prematurity	22·3	—	29·9	—
Difficulty in fixing	7·8	—	10·4	—
Breast abscess	3·9	10·3	5·2	16·8
Retracted nipples	—	1·7	—	2·8
Other causes	2·9	2·9	3·9	4·7
No. of cases	103	174	77	107

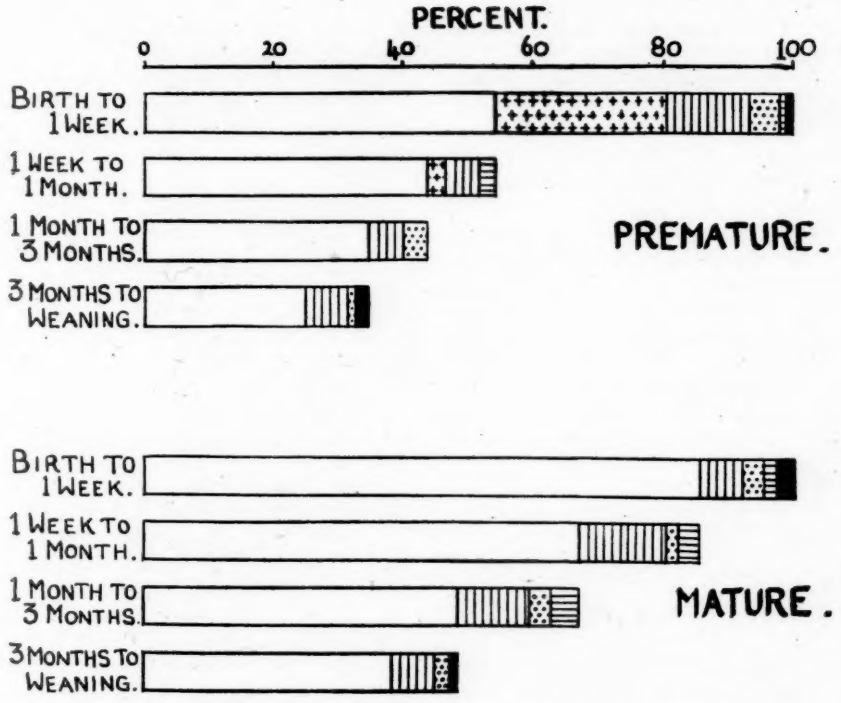

FIG. 5.—Proportion of premature and mature infants still fully breast-fed at different ages, with causes of failure to breast-feed.
Still breast feeding at end of period, outlined rectangles.
Failure to breast-feed occurring during period due to:
Prematurity and difficulty in fixing, crosses.
Insufficient lactation, vertical lines.
Illness of mother, dots.
Breast abscess, horizontal lines.
Other causes, black.

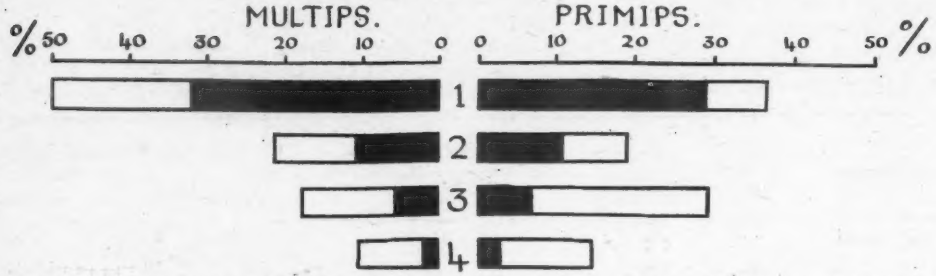

FIG. 6.—Proportion of bottle-fed infants given different artificial foods by primiparae and multiparae.
Black rectangles, medical advice.
Outlined „ , non-medical advice.
1. Fresh milk.
2. National dried milk.
3. Proprietary dried milk.
4. Additions to milk.

nurse, or health visitor, it is classed as 'medical advice,' and when given by a relative (usually the grandmother), friend, or chemist, or where the mother chose the food on her own initiative, it is classed as 'non-medical.'

Fig. 6 shows the proportion of bottle-fed infants given these foods by primiparae and multiparae, and whether on medical or non-medical advice. It shows that nearly three-quarters of the multiparae fed their infants on fresh or national dried milk, compared with just over half of the primiparae. Where medical advice was followed, these were the foods of choice, the more expensive proprietary milks and additions being given as a result of non-medical advice, and more especially by mothers of first babies.

Of those who never succeeded in breast feeding, over three-quarters continued with the artificial food recommended in hospital, or changed only on medical advice. Where failure occurred soon after leaving hospital, before three months, 60 per cent. changed to the bottle on their own initiative or on the advice of friends, whereas when breast feeding had continued successfully for longer than three months, 65 per cent. consulted a private doctor or welfare clinic before changing to the bottle.

COMPLEMENTARY FEEDING. Although complementary feeding was often recommended in cases of failing lactation, in very few cases did the mother carry this out for longer than a few weeks. Of those who never wholly fed their infants, even in hospital, a quarter attempted complementary feeding for periods longer than a week. Of those who successfully breast fed for more than three months, one-third continued with breast and bottle, most of them until weaning on to mixed diet. However, in the majority of failures which occurred between one week and three months, very few of the mothers persevered with the breast once a complementary bottle became necessary.

In short, it appears that failure in breast feeding, once it has been successfully established, most commonly occurs in the first few weeks after discharge from hospital, and certainly before the baby is three months old. The usual reason given is failing lactation, and the mother is most likely at this stage to take the baby right off the breast and substitute a bottle, commonly, in the case of a first baby, on the advice of the grandmother. If a mother succeeds in feeding her baby for longer than three months, she is usually anxious to continue, and will seek medical advice, and if possible will continue partial nursing.

A number of similar enquiries into incidence of breast feeding in different infant populations have been carried out in Great Britain, and the results of the more recent surveys are summarized in table 7.

Vitamin supplements. Enquiry was made as to the addition of vitamins A, D, and C to the diet. A minimum adequate dose of vitamins A and D was taken to be one teaspoonful of Government or other cod-liver oil, six drops of halibut liver oil or adexolin, or comparable quantities of other proprietary preparations, given daily from three months to one year.

The frequency with which a source of vitamins A and D was given varied with the type of feeding. Taking the whole sample, it was given in adequate dosage to 60 per cent., irregularly or in inadequate dosage to 20 per cent., and omitted altogether in 20 per cent. of infants. As will be seen from table 8, breast-fed infants approximated closely to this average. Of bottle-fed infants, nearly three-quarters of those fed on fresh milk received vitamins A and D, this proportion falling to less than one-half in the case of infants fed on proprietary preparations. These differences are associated with the frequency with which the various types of food were recommended by doctor or nurse, when the recommendation would be likely to be accompanied by instructions to give vitamin supplements.

A source of vitamin C, either in the form of fresh or concentrated orange juice, rose-hip syrup, or ascorbic acid tablets, was given more frequently than vitamins A and D. Of the 277 children examined, 74 per cent. had received an adequate

TABLE 7

INCIDENCE OF BREAST FEEDING AT THREE AND SIX MONTHS ACCORDING TO VARIOUS OBSERVERS

Place	Reference	Source of data	No. cases	Per cent. feeding at:	
				3 months	6 months
Liverpool ..	Robinson (1939)	Records of cases attending infant welfare clinics in 1937	439	48·0	29·0
Newbiggen-on-Sea	Hughes (1942)	Records of 95 per cent. of all births in Newbiggen, surviving for 6 months in 1940	112	32·0	19·0
Newcastle	Spence (1938)	Records of infants attending municipal welfare clinics, 1938	1,326	58·4	34·7
Ilford	Gordon (1942)	Health visitors' reports, 1940-1941	601	—	46·0
Birmingham	B.P.A. survey (Neale and others, 1943)	Health visitors' reports for:			
		1. Infants born Jan.-June, 1937	4,378	60·0	—
		2. Infants born Jan.-Mar., 1941:			
		First births	1,001	49·0	—
		Subsequent births	936	56·5	—
		3. Infants born Jan.-Mar., 1942:			
		First births	1,382	49·3	—
		Subsequent births	1,376	54·4	—

dose of vitamin C regularly, from the third month; 10 per cent. had been given irregular quantities, and 16 per cent. none at all.

Of those who had received adequate cod-liver oil or other vitamin D preparation, 84 per cent. were also given vitamin C in some form, as were 58 per cent. of those who had had no vitamin D or only inadequate amounts.

Diphtheria immunization. Of the 277 children examined, 250 had been immunized against diphtheria. Of the remaining 27, 19 were either immunized at the follow-up clinic or the mother gave assurances that the child would be taken to the private doctor. The reasons given why immunization had not been carried out were as follows: mother had not bothered, 15; disapproval of father, 6; recurrent ill-health of child, 2; waiting for school, 2; other reasons, 2.

Of those who had attended a welfare clinic regularly, 95 per cent. had been protected, but of those who did not attend a clinic only 77 per cent.

It was also noticed that 20 per cent. of those who failed to give their children any vitamin-D preparation also failed to have them immunized; this compared with 8 per cent. non-immunization amongst the others.

Sitting, standing, walking, and talking. The mother was asked at what age the child was able to: (1) sit unsupported; (2) pull himself to the standing position, and remain standing with support; (3) walk without support across a room; (4) name numerous household objects, and be able to put two or three words together such as ' more milk,' ' all gone,' ' Johnnie's ball.' The age at which single words were first acquired was not used, because of the widely differing conceptions held by mothers as to what constitutes a ' word.'

It is realized that the mothers' answers to these

TABLE 8

PERCENTAGES OF INFANTS RECEIVING COD-LIVER OIL OR OTHER SOURCE OF VITAMIN D IN THE FIRST YEAR OF LIFE, ACCORDING TO METHOD OF FEEDING

Source of vitamin D	Method of feeding				
	Breast	Fresh milk	National dried milk	Proprietary dried milk	Additions
Adequate	59·0	74·7	54·1	48·9	52·0
Inadequate	19·4	13·3	21·6	27·7	28·0
Nil	21·6	12·0	24·3	23·4	20·0
Total	100·0	100·0	100·0	100·0	100·0
No. of cases	93	75	37	47	25

questions will not be accurate, and that there will be a natural tendency to exaggerate the prowess of their offspring. There seems no reason, however, for supposing that the mothers of premature infants would be more or less accurate in their answers than the mothers of mature infants, so for the purpose of comparing development in the two groups it is legitimate to accept the mothers' statements. Indeed, any inaccuracies by the mothers would only tend to diminish the statistical significance of any differences found, so if in spite of this, significant differences are found, then these differences can be relied upon to indicate real variations between the two groups.

Although many mothers admitted that they were not certain of the dates of sitting and standing, nearly all were most definite about the age at which the child walked, and this date is probably the most reliable. Table 9 gives the average age of sitting, standing, walking, and talking in five birth-weight groups, and this is shown graphically in fig. 7. It will be seen that premature infants are definitely later in reaching all these 'milestones,' and the smaller the infant the more marked is the retardation. Among mature infants there is little variation with increase of birth weight; in fact the heaviest infants at birth appear to be a little later in time of standing and walking than the smaller mature infants.

The differences between the average ages at which premature and mature infants sat, stood, walked, and talked are as follows:

Sitting	1·4 months
Standing	2·0 months
Walking	2·0 months
Talking	4·2 months

All these differences are highly significant.

TABLE 9

AVERAGE AGE OF SITTING, STANDING, WALKING, AND TALKING, ACCORDING TO BIRTH WEIGHT

Birth weight	Average age in months			
	Sitting	Standing	Walking	Talking
4 lb. 8 oz. and under ..	9·0	13·8	16·4	26·7
4 lb. 9 oz. to 5 lb. 8 oz. ..	7·7	12·1	14·7	21·7
5 lb. 9 oz. to 6 lb. 8 oz. ..	6·7	10·1	12·9	19·1
6 lb. 9 oz. to 8 lb. 8 oz. ..	6·6	10·6	13·1	18·6
8 lb. 9 oz. and over ..	6·4	10·8	13·2	18·6

Similar figures are given by Hess and others (1934). In their group of premature infants and their full-term siblings the following differences were given between average age of sitting and walking in the two groups:

Sitting unsupported:	
girls	1·5 months
boys	1·7 months
Walking unsupported:	
girls	2·3 months
boys	3·2 months

They point out however that these differences would be appreciably minimized if allowance were made for degree of prematurity.

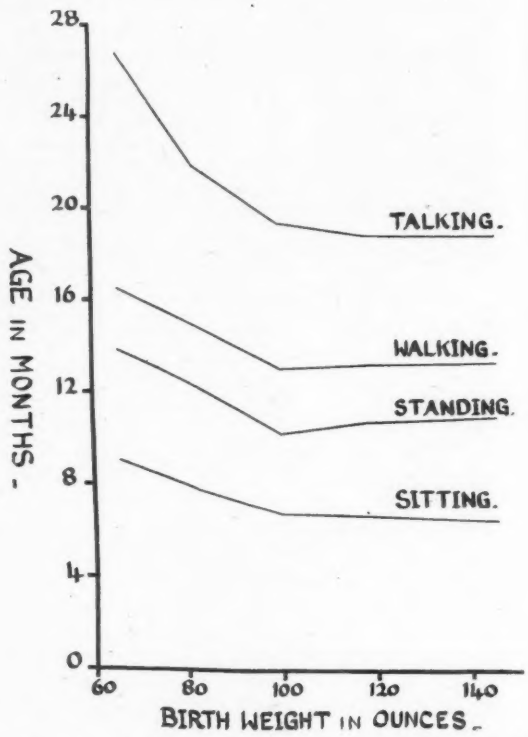

FIG. 7.—Ages at which children of different birth weight sat, stood, walked, and talked.

Morbidity rates. A full history was taken of all infections of sufficient severity to necessitate medical attention and the age at which they occurred.

The following infections were recorded: (1) measles; (2) whooping-cough; (3) bronchitis; (4) pneumonia; (5) diarrhoea and vomiting; (6) discharging ears; (7) tonsillitis; (8) others, including rubella, chicken pox, scarlet fever, diphtheria, mumps, stomatitis, gingivitis, infective hepatitis, pyelitis, and meningitis. A further group included those who had a history of recurrent bronchitis, tonsillitis, or 'chesty colds.' Children with recurrent bronchitis or tonsillitis are included once only under the appropriate heading above, as well as in this group, the age being taken as that of the first attack.

Owing to the slightly different age composition of the premature and mature groups, and to the different ages at which the infections occurred, a method of standardizing the morbidity rates has been used. Infections in each of the two groups of children were sub-classified into six-monthly groups according to the age of the child at the time of infection. The number of children at risk in each six-monthly age period was also calculated. For instance, a child aged 18 months at the time of examination was at risk in the age groups 0-6 months, 6-12 months, and 12-18 months; a child aged 24 months would also appear in the 18-24 month group, and so on. A child aged 25 months would also count as $\frac{1}{6}$ toward the 24-30 month group, because he was at risk for only that fraction of the age period.

For each six-monthly age period the specific infection rate (number of infections/number at risk) was calculated. These figures were used to compute the morbidity rates to be expected if a standard population, of the age composition of the whole sample, had the specific rates at each age of the premature and mature children. Table 10 shows the crude and the standardized morbidity rate of the premature group as a percentage of the corresponding rates for mature children. It will be seen that the crude and standardized figures do not differ greatly. Table 10 also gives the chi-squared value for the difference between the risk of infection in the premature and mature groups. Where chi squared is 3·84 or over, the difference can be considered statistically significant, the likelihood of the difference being as big as this by chance being less than 1 in 20. It will be seen that for all infections except measles and discharging ears, the majority of which were associated with measles, the morbidity rate for the premature children is higher, sometimes considerably so. The higher rate in the premature group is statistically significant for whooping-cough and pneumonia. The differences for bronchitis, recurrent bronchitis, sore throats and 'chesty colds,' and tonsillitis, though not significant individually, become so when taken together. The premature group also shows a greater number of cases of diarrhoea, but the difference from the mature group is not big enough to be significant.

It is difficult to see why measles should be so much higher in the mature group. One possible explanation is that there are a greater number of first births and only children in the premature group, thus lessening their risk of contracting measles from older siblings. If this were so one might expect to find a higher incidence of whooping-cough also in the mature group, whereas the observed difference is in the other direction. When the cases of whooping-cough were divided into those occurring in the first year of life and thereafter, it was found that 14 per cent. of the premature infants were reported as having had whooping-cough in the first twelve months of life, compared with 2 per cent. of the mature infants. The difference for whooping-cough after the age of one year was much smaller, 26 per cent. of the premature group, and 22 per cent. of the mature. In the first year of life it is notoriously difficult to diagnose whooping-cough from a persistent bronchitis or pneumonitis. It seems probable that a proportion at any rate of the excess cases of whooping-cough in the first year have been misdiagnosed. When all the specific fevers were taken together, excluding only cases of whooping-cough occurring in the first year, there was found to be little difference in the rate for premature and mature children, though the latter had the slightly higher rate.

TABLE 10

CASES OF INFECTION OCCURRING IN PREMATURE CHILDREN COMPARED WITH MATURE CHILDREN

Infection	No. of cases		Rate in premature children, taking mature rate as 100		Chi squared
	Premature	Mature	Crude	Standardized	
Measles ..	35	52	65	63	5·36
Whooping-cough ..	41	42	163	158	7·21
Bronchitis	25	38	110	109	0·17
Pneumonia	12	3	668	686	12·24
Diarrhoea	12	13	154	152	1·30
Discharging ears	5	12	69	64	0·41
Tonsillitis	10	8	208	207	2·68
Others ..	23	40	128	124	0·98
Recurrent bronchitis	17	18	157		2·10
No of children	103	174			

Fig. 8 shows specific morbidity rates for premature and mature children, in the first and second years of life respectively. During the first year of life the premature group show a much higher incidence of every infection except measles. In the second year rates for the two groups are very similar.

One may conclude from the above findings that there appears to be no marked difference in the liability of prematurely born or full-term children to contract the specific fevers of childhood, when likelihood of exposure to infection is taken into account. The larger number of cases of diarrhoea occurring in the premature group is found only in the first year of life, and is probably associated with the higher incidence of bottle feeding in this group, and possibly a lowered resistance in the early months. As regards respiratory and nasopharyngeal infections the premature children appear to be definitely more susceptible, especially in the first year of life.

These findings seem to be in agreement with the little that has been written about morbidity rates in prematurely born children. Hess and others (1934) found that the incidence of common contagious diseases of childhood did not differ in premature and full-term children, though there seemed to be a more frequent occurrence of respiratory infections, especially 'frequent colds' and pneumonia, in the premature group. Capper (1928) also found a

decreased resistance to infection, especially of the respiratory tract, in prematurely born children, chiefly in the first year of life.

Physical examination. The children were examined stripped to the waist, but the height and weight recordings were taken in light indoor clothes.

The following points were noted for every child: (1) height; (2) weight; (3) teeth—number present, number carious, whether any had been extracted, and for what reason; (4) tonsils, whether enlarged or infected; (5) cervical glands, whether palpable; (6) postural defects of the trunk or lower limbs; (7) signs of rickets; (8) any other abnormalities. In addition an estimate was made of the child's general condition. All the examinations were made by one observer, the same standards being used throughout.

TEETH. The percentage of children with no carious teeth present, and who had had none extracted because of decay, was found to be: prematurely born children, 72·5 per cent.; full-term children, 80·1 per cent. This difference is not statistically significant, the chi-squared value being 2·06.

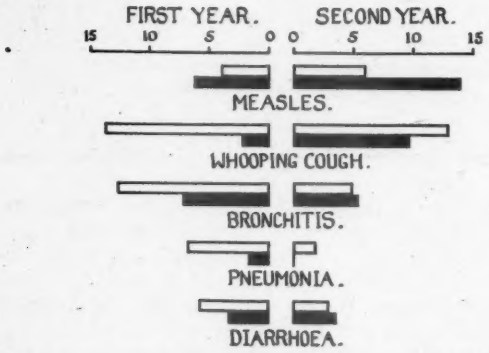

FIG. 8.—Relative morbidity rates for premature and mature children in the first and second years of life. Scale = number of cases per 100 children at risk.

NASOPHARYNGEAL INFECTION AND CERVICAL ADENITIS. Mere enlargement of the tonsils was not taken to be a sign of tonsillar infection. All cases classified as having a nasopharyngeal infection showed obviously infected tonsils, or a chronic nasal discharge, or both. Nearly all these cases also showed marked enlargement of the cervical glands. In most cases of glandular enlargement without obvious nasopharyngeal infection there was a history of sore throats or recurrent colds. In two cases the cervical adenitis was considered to be tubercular, and these cases have not been included in table 11, which shows the incidence of nasopharyngeal infection and cervical adenitis in premature and full-term children. As will be seen, in spite of the higher incidence of acute tonsillitis and recurrent sore throat recorded in the histories of the premature group, little difference was found between them and the mature group on examination. A slightly larger number of prematurely born children had had tonsils removed.

RICKETS. Very few cases of gross rickets were seen in either group. Of the premature children, 2·0 per cent., and of the mature children 4·7 per cent. showed signs of old rickets of a moderate or severe degree, that is, showing obvious enlargement of osteochondral junctions, and epiphyses of wrist and ankle. The larger number of cases in the mature group is probably accounted for by the lower percentage receiving an adequate supply of cod-liver oil, or other vitamin D preparation, during the first year of life.

Grooving and flaring of the lower ribs, without any other sign of rickets, was noted in 19·6 per cent. of the premature children, and in 16·7 per cent. of the mature children, but this is not considered to be a reliable sign of rickets and it may occur with any type of respiratory embarrassment, such as chronic bronchitis or asthma.

TABLE 11

INCIDENCE OF NASOPHARYNGEAL INFECTION AND CERVICAL ADENITIS IN PREMATURE AND FULL-TERM CHILDREN

Birth weight	Percentage showing:	
	Nasopharyngeal infection	Cervical adenitis
Premature ..	5·0	18·6
Mature	4·3	25·9

GENERAL CONDITION. The children were classified in three groups according to the following criteria:

1. Good. In these cases the child appeared to be of normal height and weight for age, and in a good state of nutrition. No obvious abnormalities were found on examination, and the mother stated that the child enjoyed good health, had made a complete recovery from such illnesses as had occurred, and was active and alive in general behaviour. Enlargement of the tonsils with slight enlargement of the cervical glands was not considered serious enough to remove a child from this category.

2. Poor. These children showed one or more of the following signs: obvious malnutrition, some gross pathological condition affecting general health (such as chronic bronchitis, congenital heart disease, gross nasopharyngeal infection); a history of constant ill health. Typically the mother would say that the child was always ailing, acquired infection easily and made a slow recovery from such infections, had a poor appetite, tired easily, and had no 'life.'

3. Fair. In between these two extremes came the children who did not measure up to the standards of group 1, and yet whose condition was not so bad as to be classed as poor.

TABLE 12

GENERAL CONDITION ACCORDING TO WEIGHT AT BIRTH

General condition	Birth weight				
	4 lb. 8 oz. and under	4 lb. 9 oz. to 5 lb. 8 oz.	5 lb. 9 oz. to 6 lb. 8 oz.	6 lb. 9 oz. to 8 lb. 8 oz.	8 lb. 9 oz. and over
	Per cent.	Per cent.	Per cent.	Per cent.	Per cent.
Poor ..	20·0	16·9	3·0	3·5	—
Fair	28·0	42·9	48·4	32·5	4·3
Good ..	52·0	40·2	48·4	64·0	95·7
Total ..	100·0	100·0	100·0	100·0	100·0
No. of cases ..	25	77	33	114	23

Table 12 shows the proportion of cases falling into each category according to their weight at birth. It will be seen that with increasing weight at birth the proportion of children classified as poor falls steadily, with a corresponding increase in those classified as good. Of those who weighed 4·5 lb. or less at birth, 20 per cent. were considered to be in poor general health, while at the other extreme, of those whose birth weight was over 8·5 lb. 96 per cent. reached the highest standard. These differences according to birth weight are highly significant. The chi-squared value is 38·1, and the odds against this occurring by chance are more than 130,000 to one.

HEIGHT AND WEIGHT. In considering height and weight according to weight at birth, the children have been divided into five birth weight groups:

4 lb. 8 oz. and under
4 lb. 9 oz. to 5 lb. 8 oz.
5 lb. 9 oz. to 6 lb. 8 oz.
6 lb. 9 oz. to 8 lb. 8 oz.
8 lb. 9 oz. and over

For each birth weight group the regression equation has been calculated of weight on age, and height on age; this being the equation to the straight line which best describes the association between these characteristics. The equations are set out in table 13 and graphically in figs. 9 and 10. From these equations one can calculate what would be the average height and weight at any age for each birth weight group as shown in tables 14 and 15. These tables also give the average weight and height of children of the same ages, as compiled from Holt's figures by Sheldon (1946). It has been assumed that the relation between weight or height and age can adequately be expressed by a straight line, whereas in actual fact the rate of growth is greater at the earliest ages, but for the purpose of comparing growth in different birth-weight groups this can legitimately be ignored. Fig. 9 shows that at any given age, average weight rises steadily with increasing birth weight. At two years there is a difference of 5 lb. in average weight between the smallest and the largest birth-weight groups; the difference is 6 lb. at three years and 7 lb. at four years.

Fig. 10 demonstrates the same trend as regards height, though the differences between birth-weight groups are not nearly so marked.

TABLE 13

REGRESSION EQUATIONS FOR HEIGHT AND WEIGHT ON AGE IN DIFFERENT BIRTH WEIGHT GROUPS

Birth weight	
1. 4 lb. 8 oz. and under ..	W=5·76A+257, H=0·24A+27·15
2. 4 lb. 9 oz. to 5 lb. 8 oz.	W=5·53A+276, H=0·25A+27·48
3. 5 lb. 9 oz. to 6 lb. 8 oz.	W=5·70A+290, H=0·21A+29·76
4. 6 lb. 9 oz. to 8 lb. 8 oz.	W=6·67A+283, H=0·28A+27·18
5. 8 lb. 9 oz. and over ..	W=7·59A+289, H=0·30A+27·24

W=Weight in ounces
H=Height in inches
A=Age in months

Very few surveys have been carried out in this country on the progress and development of the prematurely-born child, after the first year of life, but numerous observers on the Continent and in the United States come to very different conclusions as to the progress of these children. For instance Capper (1928) after a detailed study of 103 prematurely-born children between the ages of one and seventeen years writes, 'The fate of immature children is not enviable; almost one half of them die during the first year of life. Of those that remain alive the majority are physically as well as mentally underdeveloped.' Whereas Hess and others (1934), from an equally careful study of 250 premature infants between one and seven years, concluded that by the age of four years the prematurely-born child had caught up in every respect with the mental and physical development of the full-term child.

The discrepancies seem to be due largely to different methods of selecting the sample, and whether a comparable control group of full-term children was included in the study. Capper selected his cases from 23,000 hospital records. 613 were picked who seemed from their medical history to have been prematurely born, though only 437 were verified by checking the birth weights with the maternity departments concerned. From this number he obtained 103 children for re-examination. It is obvious that in the method of selection there was a bias in favour of including those with a history of early difficulties, and all the cases had for some reason passed through hospital. These

TABLE 14

AVERAGE WEIGHT AT DIFFERENT AGES, ACCORDING TO WEIGHT AT BIRTH, CALCULATED FROM THE REGRESSION EQUATIONS

Birth weight	Average weight in lbs.		
	2 years	3 years	4 years
4 lb. 8 oz. and under ..	24·7	29·0	33·3
4 lb. 9 oz. to 5 lb. 8 oz. ..	25·5	29·7	33·8
5 lb. 9 oz. to 6 lb. 8 oz. ..	26·7	31·0	35·2
6 lb. 9 oz. to 8 lb. 8 oz. ..	27·7	32·7	38·1
8 lb. 9 oz. and over ..	29·5	35·1	40·8
Standard for normal children, adapted from Holt and McIntosh (1940) ..	28·0	33·0	37·0

TABLE 15

AVERAGE HEIGHT AT DIFFERENT AGES ACCORDING TO WEIGHT AT BIRTH, CALCULATED FROM THE REGRESSION EQUATIONS

Birth weight	Average height in inches		
	2 years	3 years	4 years
4 lb. 8 oz. and under ..	32·9	35·8	38·7
4 lb. 9 oz. to 5 lb. 8 oz. ..	33·2	36·5	39·5
5 lb. 9 oz. to 6 lb. 8 oz. ..	34·8	37·3	39·8
6 lb. 9 oz. to 8 lb. 8 oz. ..	33·9	37·3	40·6
8 lb. 9 oz. and over ..	34·4	38·0	41·6
Standard for normal children adapted from Holt and McIntosh (1940) ..	33·0	37·0	40·0

children were compared, not with a control group of full-term infants selected from the same records, but with accepted standards for normal healthy children. It is hardly surprising that the premature group compared unfavourably.

Those observers who have compared a random sample of premature infants with various accepted standards of normality, usually agree that prematurely-born children show to a greater or lesser degree a lower average height and weight. Von Sydow (1936) examined a series of ninety-eight premature children between the ages of three and nine years, and found a certain degree of underdevelopment as compared with the general population. Brander (1938, 1941) followed up a series of nearly 400 premature infants until the end of school age, and came to the same conclusion. On the other hand Hess and others (1934) and Schultze (1939), using as their control group brothers and sisters of the premature infants in question, both concluded that there was no fundamental difference as regards height, weight, or general development after the first few years of life. It should be noted that Hess's group of premature children had been carefully supervised by doctors and social workers throughout the period under review, as had a group quoted by Levine and Gordon (1942), which also showed no striking difference from a comparable full-term group.

In this country Asher (1946) recently examined a series of 217 prematurely-born children between the ages of one and six years and found them to be below average weight at all ages compared with standard figures quoted by Holt and McIntosh (1940). Illingworth (1939) compared a random

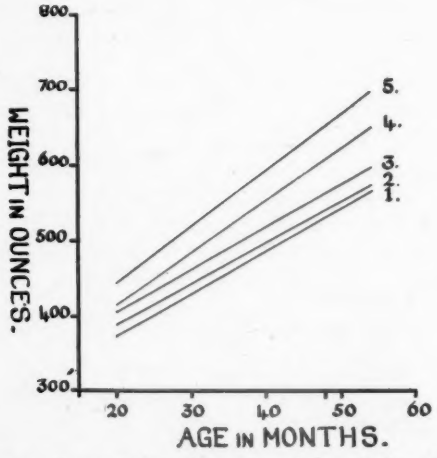

FIG. 9.—Regression lines showing relation between weight and age for five birth weight groups.

(1) 4 lb. 8 oz. and under; (2) 4 lb. 9 oz. to 5 lb. 8 oz.; (3) 5 lb. 9 oz. to 6 lb. 8 oz.; (4) 6 lb. 9 oz. to 8 lb. 8 oz.; (5) 8 lb. 9 oz. and over.

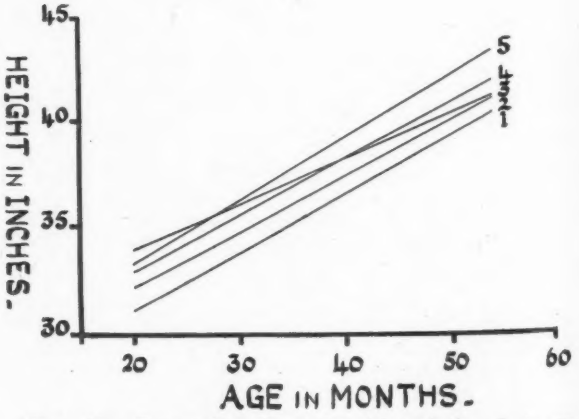

FIG. 10.—Regression lines showing relation between height and age for five birth weight groups.

(1) 4 lb. 8 oz. and under; (2) 4 lb. 9 oz. to 5 lb. 8 oz.; (3) 5 lb. 9 oz. to 6 lb. 8 oz.; (4) 6 lb. 9 oz. to 8 lb. 8 oz.; (5) 8 lb. 9 oz. and over.

sample of 152 children between the ages of one and eleven years who weighed 5·5 lb. or less at birth, with a similar group weighing 8·5 lb. or more at birth, all of them being children attending the out-patient department of Great Ormond Street Hospital, London. He found that the premature children were under weight as compared with the control group.

In interpreting these different findings the most important question to decide is whether the fact of premature birth alone places the child under a permanent handicap, or whether it is rather that the unfavourable factors which acted on the mother, causing the premature delivery, continue to act on the child after birth. There is ample evidence to support the theory that premature birth is closely associated with bad economic and social conditions. The Royal College of Obstetricians and Gynaecologists suggest in their report on the National Maternity Service (1944) that prematurity is largely due to defective maternal diet. This was corroborated by Cameron and Graham (1944), who examined the diets of one hundred mothers of premature and one hundred mothers of mature infants, and found the food intake to be qualitatively and quantitatively better in the latter group. Baird (1945) found the incidence of prematurity among women of poor social class in hospital to be twice as high as that among private patients in a nursing home. The Registrar General for England and Wales (1931) found that deaths of infants attributed to premature birth increased as one descends the social scale, and were about twice as common among babies of unskilled labourers as among those of Social Class 1. Woolf (1947) showed that neonatal death rates and death rates from congenital causes, of which prematurity forms the most important single cause, are very highly correlated with poverty indices. It seems reasonable to suppose that these economic handicaps would continue to act on the premature infant after birth, and this supposition is strengthened by the fact that where brothers and sisters from the same environment are used as the control group very little difference is found after the first few years of life. Equally, where good post-natal conditions exist and adequate supervision, the premature infants surviving the first year of life quickly caught up with comparable full-term children. It is hoped to amplify this theme in a further paper, in which the social background of a group of premature and mature infants will be studied and compared.

Behaviour problems. Every mother was questioned as to the general behaviour of her child, and whether there were any problems in social adaptation or habit formation. Questions were asked about feeding and sleeping habits, bladder and bowel control, attitude to children, parents, and other adults. No attempt was made to obtain detailed case histories, only obvious behaviour disorders being recorded.

Twenty-four out of 102 mothers of prematurely born children (23 per cent.), and 25 of 170 mothers of full-term children (15 per cent.) reported behaviour problems. Feeding problems were by far the commonest complaint, and these have been considered separately.

In most other cases the mother stated that the child was generally difficult to manage, was ' out of hand,' exhibited temper if thwarted, was over-dependent on his parents, and had difficulties in his relations with other children or adults. In a minority of cases there was one outstanding symptom or symptom complex which was considered to be functional in origin. For example, one child suffered for two years from extreme constipation which was entirely cured by treatment at a child guidance clinic. A boy with crippling asthma always had an attack following parental quarrels, which were frequent. Another had frequent attacks of cyclical vomiting provoked by excitement, and particularly by his failing to get his own way. In this case the child lived in crowded conditions with seven adults, including two grandmothers, and was the centre of attention of the whole household.

In most cases it was obvious that the mother had little control over the child, who was being mismanaged at home. Many suffered from bad housing conditions or from having to live with grandparents, where authority was divided between the mother and grandmother. The majority were difficult to examine and needed much reassurance before permitting themselves to be undressed. In a few cases examination was impossible because of screaming, kicking, and other manifestations of temper.

FEEDING PROBLEMS. Here the mother stated that the child had a poor appetite and had to be coaxed to eat by various devices. In all cases, to a greater or lesser extent, meals had become a struggle between the child and his parents.

It was noticeable that the general health of children with feeding problems was inferior to those without such difficulties, and therefore a comparison was made between the incidence of feeding disorders in children of good, fair, and poor general health, for both premature and mature children.

The results are shown in table 16. A striking difference is seen between the incidence of feeding problems in those in poor and good health for both premature and mature children. Among the premature children the difference between the group classified as in poor general health and that classified as ' fair ' is highly significant, the chi-squared value being 20·81; the difference between ' fair ' and ' good ' is also significant, with a chi-squared value of 4·77. In the mature group the two

similar comparisons also show significant differences, here the chi-squared values are 18·70 and 4·16 respectively.

Although both premature and mature groups show the same trend, it will be seen that the incidence of feeding problems in the former is higher in every health category. The differences between the premature and mature rates in each sub-group when taken together are statistically significant, a combined probability test giving a t value of 3·125. A t value of 2·0 would be significant according to the accepted standard of a probability of 0·05. It appears, therefore, that though there is a positive association between feeding problems and poor health irrespective of birth weight, there is also a significantly higher rate among prematurely born children as compared with full-term children, quite apart from their state of health.

TABLE 16

PERCENTAGE OF PREMATURE AND MATURE CHILDREN WITH FEEDING PROBLEMS ACCORDING TO THEIR GENERAL HEALTH

	General health			
	Poor	Fair	Good	Total
Premature ..	83·3	20·0	4·6	24·5
Mature	60·0	3·7	—	2·9
Total	78·3	10·6	1·3	
No. in group ..	23	94	155	

OTHER BEHAVIOUR PROBLEMS. Table 17 shows the incidence of other behaviour disorders in premature and mature children according to their state of general health.

Here the difference between premature and mature is much smaller and is not statistically significant, the chi-squared value being only 1·77.

However, the incidence of behaviour disorder is over twice as high in the ' poor ' health group as in the ' fair,' and three and a half times the rate among those in good general health. The difference between the ' poor ' and ' fair ' groups is statistically significant (chi-squared value = 5·37); the difference between the ' fair ' and ' good ' groups is not significant (chi-squared value = 1·45), but the difference is in the same direction and very suggestive.

Summing up these findings one may say that both feeding problems and other behaviour disorders as a whole appear to be more common in children whose general health is poor, and that as regards feeding problems there is a preponderance of cases among prematurely born children. No conclusions are drawn as to whether the behaviour disorder results from the poor health or vice versa.

Hess et. al. (1934), in their study of premature children and their full-term siblings, observed that ' prematurely born children more frequently evidence dependency reactions in relation to their mothers, are somewhat less adequate in their earliest social responses, and display temper more frequently.'

Summary

This paper comprises Part 4 of a series of studies in prematurity based on births in the Simpson Memorial Pavilion, Edinburgh, during the years 1943-1945 inclusive. It is divided into two sections: (1) a comparison of the medical history of surviving premature and mature infants before discharge from hospital; and (2) an account of a follow-up examination of a sample of prematurely-born children, and a control group of full-term children.

TABLE 17

PERCENTAGE OF PREMATURE AND MATURE CHILDREN WITH BEHAVIOUR DISORDERS (OTHER THAN FEEDING PROBLEMS), ACCORDING TO THEIR GENERAL HEALTH

	General health			
	Poor	Fair	Good	Total
Premature ..	38·9	25·0	6·8	19·6
Mature	40·0	11·1	13·5	13·5
Total	39·1	17·0	11·6	
No. in group ..	23	94	115	

SECTION 1: PROGRESS IN HOSPITAL

Infection rates in the first ten days of life were considered. Infants of 3·5 lb. or under at birth had a much higher rate of septic skin infection and conjunctivitis than larger babies. The incidence of thrush fell steadily with increasing birth weight, this being associated most probably with increase in breast feeding. The smallest infants appeared relatively immune to gastro-enteritis, this probably being due to their isolation from the main nursery.

Comparative rates are also given for other pathological conditions occurring in infants of different birth weights.

SECTION 2: PROGRESS IN EARLY CHILDHOOD

A sample of 277 children between the ages of one-and-a-half and four-and-a-half years returned for re-examination: 103 were prematurely born, and 174 were full-term children.

The following points arising out of information given by the mother were considered:

1. Feeding in the first year. The incidence of breast feeding was found to vary with birth weight and parity. Causes of failure in breast feeding, and the artificial foods chosen by different types of mothers, are discussed.

2. Administration of vitamin supplements.
3. Diphtheria immunization.
4. Milestones in development. A significant difference was found between the ages at which premature and mature infants sat, stood, walked, and talked. The smaller the infant, the more marked was the retardation. Among mature infants there was little variation with increase of birth weight.
5. Morbidity rates. No marked difference was found between the liability of premature and mature children to contract the specific fevers of childhood. Prematurely-born children showed a significantly higher incidence of nasopharyngeal and respiratory infection, this being especially marked in the first year of life.
6. Behaviour disorders. Twenty-three per cent. of the premature, and 15 per cent. of the full-term children were reported as having behaviour problems. Feeding problems were the most common. These, as well as behaviour disorders in general, were positively associated with poor health. There was a preponderance of feeding problems amongst the premature group.

The following findings were made from the physical examination:

1. No significant difference was found between premature and full-term children in the incidence of dental caries, nasopharyngeal infection, cervical adenitis, and rickets.
2. The children were classified as to their general condition into three groups: poor, fair, and good. With increasing birth weight the proportion of children classed as 'poor' fell steadily, from 20 per cent. in those of 4·5 lb. and under at birth, to none in those weighing over 8·5 lb. There was a corresponding increase in those classed as 'good.' These differences are highly significant.
3. Height and weight. Regression equations were calculated of height on age and weight on age, for each of five birth-weight groups. At any given age, average weight was found to rise steadily with increasing birth weight. The same trend was observed for height, though the differences were not so striking.

The work of other observers in this field is discussed, and the suggestion is made that the differences found after the first few years of life between prematurely-born and full-term children, as regards height, weight, and general development, are due largely to environmental factors, being the same adverse conditions as originally acted on the mother to produce the premature delivery.

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ON THE CAUSE OF NUCLEAR JAUNDICE IN NEONATAL SEPSIS WITH JAUNDICE

BY

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The discovery of the Rhesus factor, which plays such an important part in the explanation of haemolytic disease in the newborn, has also drawn attention to the question of nuclear jaundice and suggested new ideas about its pathogenesis. The possibility has been considered that the erythrocytes which agglutinate as a consequence of the antigen-antibody reaction, form agglutination-thrombi in the capillaries of the brain (Wiener, 1946), but this conception is not generally accepted (Parsons, 1947). It is agreed that nuclear jaundice is produced by bile-staining of previously damaged tissue. However, no explanation can be given of the fact that in this process certain nuclei and cell masses of the brain are almost constantly stained, whereas others remain unstained. One explanation assumes that differences in maturity of the brain nuclei at birth are important, while differences in the blood supply of different parts of the brain have been considered by other observers to be significant in this connexion (Biemond and Van Creveld, 1937).

Authors differ in their estimates of the frequency of the occurrence of nuclear jaundice. Cappell (1947) found it in about 30 per cent. of children who died from icterus gravis, while 12 per cent. of the survivors showed neurological symptoms.

Nuclear jaundice does not occur in congenital acholuric jaundice, nor as a rule in other forms of jaundice of the newborn which are not caused by Rh immunization. However, sometimes nuclear jaundice has been observed after septic jaundice of the newborn. In these cases the first question should be whether Rh immunization can be demonstrated. We have considered this in two recent cases, and have also established the Rh status of the parents of two infants who died some years ago of nuclear icterus associated with septic jaundice. An account of these two children was published in 1937 before the discovery of Rh groups (Biemond and Van Creveld, 1937).

Case Histories

Case 1 concerns both parents of the child E.C., described in 1937. This child was born in 1933 and was the sixth of healthy parents. The first three children were born at full term and were healthy. Then twins were born, of which one is alive and healthy, the other having died at home at the age of three days: the exact cause of death is unknown, but the infant may have been icteric soon after birth.

According to the parents the sixth child, our patient, became jaundiced soon after birth. When examined in hospital at four days old it had an umbilical infection and severe jaundice, and by the next day there were clinical symptoms of nuclear jaundice. On the fourth day of life the blood did not show any abnormality indicative of icterus gravis neonatorum.

Between 1933 and the end of 1944 the mother did not become pregnant. In August, 1945, she gave birth to a full-term child who on the second day of life was admitted to the hospital, where it died next day. The child became yellow on the second day of life, and jaundice quickly increased. The urine was normal in colour. There was a praecordial systolic murmur. The spleen was palpable, and the liver edge could be felt. The blood contained fifteen nucleated red cells per 1,000 erythrocytes. Autopsy showed nuclear jaundice. It seems probable that this was a case of icterus gravis neonatorum. In this connexion we were greatly interested in the Rh tests on the parents, whose luetic reactions were negative. Repeated examination of the serum of the mother showed Rh agglutinins (titre 1:4) as well as incomplete Rh antibodies (titre 1:16). So it is fairly certain that the child who died in 1945 suffered from icterus gravis neonatorum; and notwithstanding the fact that in the child who died in 1933 the diagnosis of septic jaundice had been made on clinical findings, it is very probable that here also Rh immunization played a part in the occurrence of the nuclear jaundice. The fact that the morbus haemolyticus becomes manifest in the fourth or fifth pregnancy (which here cannot be established with certainly) need not weigh against this diagnosis (de Bruyne, 1946).

Case 2 concerns the mother of the child M.H. described in 1937. The father, who suffered from bronchial asthma, has since died. The first two children were normal. The third, M.H., was born

in 1934 spontaneously, at full term, and was not jaundiced at birth but shortly afterwards became icteric. When taken into the hospital on the fourth day of life the baby was deeply jaundiced; the umbilicus was thickened, red, and infiltrated; above the umbilicus there was infiltration of the abdominal wall. The child was somewhat lethargic. The liver was slightly enlarged, the spleen was not palpable. The urine was dark brown and contained bilirubin. Already on admission there was rigidity of both arms. During the following days the clinical picture of nuclear jaundice became more evident. The blood showed no anaemia and no nucleated red cells. The mean diameter of the erythrocytes was somewhat decreased. The luetic reactions in the blood of parents and child were negative.

The mother had two more pregnancies between 1938 and 1940. In none of these children was there any indication for the diagnosis of foetal erythroblastosis. The first child was a girl with Mongolian idiocy, who was not icteric or anaemic in the neonatal period. The second child, according to the mother, had a spina bifida, and died after some days.

The mother was Rh-negative, and no direct agglutinins could be demonstrated, but incomplete Rh antibodies were detected in the low titre of 1:4. Though in this case the clinical symptoms did not point to nuclear jaundice caused by erythroblastosis foetalis, it is very remarkable that incomplete antibodies were present in the mother's serum after such a lapse of time. On repetition of the test the observation was confirmed.

Case 3. H. is the second child of healthy parents. The first child is 14 years old; after this child the mother had two pregnancies, each ending in a miscarriage after a three months' gestation. The second child showed no symptoms until forty-eight hours after birth, when parents and nurse observed that it had become icteric. The next day it had slight facial twitches, and on the fourth day the condition became worse: the child did not suck, had a temperature of 105° F. (40·5° C.), and showed opisthotonus. When it came into the hospital at the age of four and a half days, it was intensely icteric, and showed the clinical picture of nuclear jaundice: opisthotonus, 'mumbling' of the lips, marked hypertonia of the extremities with clasp-knife phenomenon, and slow mowing movements of the arms. The liver extended two fingerbreadths below the costal margin; the spleen was slightly enlarged. The umbilical cord had already fallen off and the umbilicus showed slight redness and serous secretion. Examination of the blood showed haemoglobin 98 per cent.; erythrocytes 3,660,000 per c.mm.; leucocytes 15,600 per c.mm. (5 per cent. rod-shaped leucocytes, 54 per cent. polymorphonuclear leucocytes, 35 per cent. lymphocytes; 6 per cent. monocytes; marked toxic granulation). No nucleated red blood corpuscles were seen. Blood culture was negative. The next day the clinical symptoms of nuclear jaundice were still very marked. The umbilicus now showed signs of infection; the wound was treated with penicillin. While the clinical diagnosis seemed to be septic icterus with nuclear jaundice, the examination of the blood groups showed that Rh immunization of the mother had taken place. The father's blood group was B CDe, the mother's A ~~CDe~~ cde, and the child's A CDe. On the fifth day after birth the direct Coombs-test with the child's erythrocytes was positive. In the mother's serum no Rh-agglutinins were found but incomplete anti-D antibodies were present to a titre of 1:64.

Case 4. C. van V. was the third child of healthy parents. Two elder children were healthy and had no neonatal jaundice. This child became slightly icteric on the second day of life without any other symptom of disease. The jaundice gradually increased. On the fifth day the general aspect of the child became worse: he did not suck; he vomited, was lethargic and suffered from attacks of sudden crying during which arms and legs were spastically extended. No real convulsions were observed.

When the child was admitted to the Children's Clinic of the Binnengasthuis the skin had an intense orange-yellow colour. The baby cried a good deal. The abdomen was slightly swollen. The umbilical cord had already fallen off. The slightly protruding wound of the umbilicus was inflamed and showed on one side a slight infiltration of the skin. The liver and spleen were not palpable.

Examination of the blood showed: haemoglobin 142 per cent.; erythrocyte count 5,380,000 per 100 c.mm. of blood; reticulocyte count 23 per 1,000; leucocyte count 15,500 per c.mm. (metamyelocytes 6 per cent., rod shaped leucocytes 11 per cent., polymorphonuclear leucocytes 52 per cent.; lymphocytes 28 per cent.; normoblasts 2 per 100 leucocytes). The blood groups appeared to be: father A Rh-positive, mother O Rh-positive, child A Rh-positive. Later on all three appeared to belong to the subgroup CDe. A blood culture of the child remained sterile.

The patient was treated with 60,000 units of penicillin a day, given in 6 intramuscular injections, and by mouth with 1 g. sulfadiazine daily in eight divided doses, while the umbilicus was dressed with penicillin. During the stay in the hospital the tonic extension-cramps of short duration continued, while in the intervals hypertonia of the muscles was present.

Lumbar puncture showed yellow clear fluid under increased pressure. The Nonne reaction was slightly positive, that of Pandy strongly positive. There was one polymorphonuclear neutrophilic leucocyte per c. mm. and 8 lymphocytes.

Next day the general condition remained about the same; the infected umbilicus quickly improved. On the eighth day of life the temperature, which had been normal, suddenly rose to 105·6° F. (40·8° C.).

The child did not suck, became cyanotic, and died.

The autopsy was performed by Dr. Witsenburg, of Dr. R. van Dam's pathological department.

LIVER. The capillaries were greatly dilated, with much bile pigment between the hepatic cells. The portal spaces contained many leucocytes.

No myeloid tissue was seen.

SPLEEN. The spleen contained much blood; there were small follicles without reactive centres.

UMBILICUS. The umbilicus was rich in vessels, around which were accumulations of leucocytes. On the surface there were necrotic foci without signs of reaction. The cord was separated.

BRAIN. There was clear, icteric staining of the corpus striatum, hippocampus, and dentate nucleus.

DISCUSSION. In this case the nuclear jaundice, based on clinical, haematological, serological, and pathological findings could not be explained by Rhesus immunization.

However, in view of the blood groups of the parents, immunization by group A cannot totally be excluded. The titre of the agglutinins in the serum of the mother was established three months after the death of the child: this proved to be 1:512, a rather high value but not definite proof of immunization. The titre of antibodies in the maternal serum can, however, decrease quickly after parturition. The possibility therefore exists that directly after the birth of the child this titre was much higher. If we discard the possibility of an A immunization, we have to accept that in this case the disease was caused by septic infection originating from the umbilicus.

Comment

In a former publication (Biemond and Van Creveld, 1937), the cases of two infants with nuclear and umbilical infection were presented. The argument that in the families of both children no cases of erythroblastosis foetalis had occurred has now lost its value in one case (case 1). It remains remarkable that in both cases erythroblastaemia and increase of the mean diameter of the erythrocytes were absent. The opinion expressed at that time that these cases proved that nuclear jaundice occurs in septic jaundice of the newborn as well as in erythroblastosis appears now to be less securely founded. Indeed, in three of the four cases communicated here we obtained arguments telling more or less in favour of Rh immunization; in the fourth case no indications for this conception could be found. Though we have to accept in three of the four cases the existence of Rh immunization, we cannot neglect the infection which was present in all of them. It is difficult to tell how often infection is present in cases complicated by nuclear jaundice, but in future signs of infection should be looked for in every case. Does infection perhaps promote nuclear jaundice in the presence of icterus gravis? It is remarkable how frequently, especially in the cases accompanied by nuclear jaundice, the icterus gravis itself takes a less characteristic course, as for instance a retarded beginning of the icterus, absence of erythroblastaemia, etc.

Summary

In two cases of septic icterus in the newborn combined with nuclear jaundice previously described, the examination of the parents and the clinical anamnesis of the children born since 1937 showed that Rh immunization was fairly certain in the first case; while in the second, where no clinical indications for this conception were present, the blood examination also spoke to a certain degree in favour of a Rh immunization. In a third case recently observed the Rh relations in parents and patient also pointed to a Rh immunization. In a fourth case, Rh tests of the parents and patient did not point to Rh immunization, but the possibility of immunization by blood group A could not be excluded.

We want to thank Dr. van Loghem in Amsterdam and Dr. Weyers in the Hague most cordially for their kind co-operation in determining the Rh tests in these cases.

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CAUSE AND SIGNIFICANCE OF SEASONAL VARIATION IN THE HÆMORRHAGIC TENDENCY IN THE NEWBORN

BY

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The discovery of vitamin K led to the hope that its use would be an important step forward in the prophylaxis of haemorrhagic disease of the newborn and possibly also of intracranial haemorrhage. Its value in the latter, however, has proved to be extremely limited (Willi, 1942; Dyggve, 1947). It was, therefore, felt desirable to search for other possible factors concerned with haemorrhagic states in the newborn.

During a period of five years, over 10,000 newborn infants were investigated at the University's Obstetrical Clinic at Budapest, and a definite seasonal variation in the incidence of melaena, cerebral haemorrhage, and cephalhaematomata was observed (Kerpel-Fronius, 1944). Such a seasonal incidence has for many years been recognized in the case of melaena neonatorum, with a peak period in winter and spring (McCollum, 1928; Hirano, 1932; Kepila and Leppo, 1937; Winkler, 1939). This paper concerns 300 newborn infants with cerebral haemorrhage or cephalhaematomata in whom a similar seasonal incidence was observed.

Waddell and Lawson (1940), from an analysis of deaths due to birth-injury, found the highest mortality in the winter months. It may therefore be assumed that the newborn infant possesses an efficient anti-haemorrhagic factor in the summer and autumn and that this factor diminishes considerably in winter and spring. It has been calculated that the protective influence of the summer is so potent that if all the 10,000 infants seen at the Budapest clinic had been delivered during the summer months the incidence of cerebral haemorrhage would have been halved (Kerpel-Fronius, 1944).

Factors Relevant to Seasonal Variation

In considering the problems of haemorrhagic disease of the newborn in relation to seasonal variations there are three factors which are relevant: firstly the degree of trauma, secondly the efficiency of the clotting mechanism, and thirdly the fragility of the capillaries. The first cannot be the cause of any seasonal variation. The second certainly can. The most marked prothrombin deficiency has been observed during winter and spring (Waddell and Lawson, 1940; Lehmann, 1944). That the third factor may also be causative is suggested by the frequency of conjunctival haemorrhages. These haemorrhages are petechial and originate from rupture of capillaries during labour and are presumably independent of fluctuations in prothrombin level. They were observed in 196 infants of 1,008 born in one year and showed a high peak in winter and spring, closely parallel to the incidence of cerebral haemorrhage and cephalhaematomata, so that it may be assumed that capillary fragility may also play an important part in the origin of the latter.

Capillary Fragility

To obtain further information about the influence of the seasons on capillary fragility, 233 healthy children were examined in one year and the data obtained are shown in table 1.

TABLE 1
SEASONAL INCIDENCE OF CAPILLARY FRAGILITY IN CHILDREN

	Negative pressure cm. Hg.					
	10	15	20	25	30	
Months	Number of cases					Percentage of children with fragile capillaries
Jan., Feb.	2	8	13	9	8	25
Mar., April	4	13	6	8	8	43·5
May, June	5	5	10	13	6	25·6
July, Aug.	1	3	21	11	4	10
Sept., Oct.	1	4	17	10	5	13·5
Nov., Dec.	1	4	8	12	13	13·1

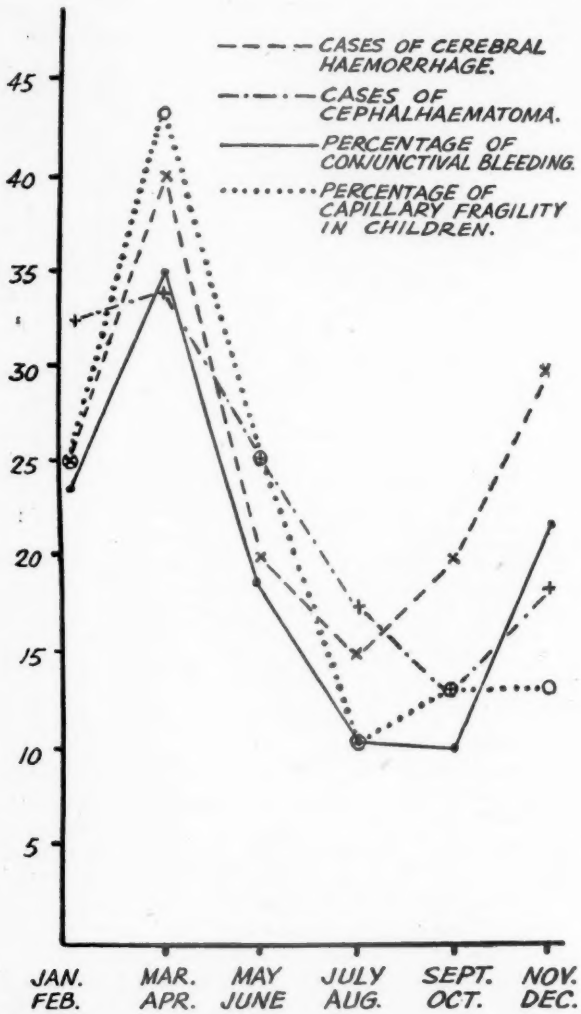
Borbély's negative pressure-suction method was used (Borbély, 1930) and the smallest negative pressure that caused visible petechiae was determined. Haemorrhage occurred in all cases at negative pressures varying between 10 and 30 cm. Hg. Pressures below 15 cm. may be considered low. In thirty-two out of fifty-one cases of low pressure, Rumpel-Leede's test, using a positive pressure of 40 mm. Hg. for 30 minutes, was equally positive.

In 182 cases with resistant capillaries, as judged by the suction test, Rumpel-Leede's test was invariably negative also.

The evidence presented in table 1 shows a decided seasonal variation in capillary fragility. The number of children with fragile capillaries increases in winter and shows a peak in early spring. The two extremes were found in March and August. In the month of March petechial bleeding, using negative pressures below 15 cm. Hg., appeared on the skin of every second child, in August only on every twentieth. This is in agreement with some similar observations by Roberts et al. (1937).

The figure shows the curves of the seasonal incidence of 150 cases of cerebral haemorrhage and 152 cases of cephalhaematoma as compared with the curve of the incidence of fragile capillaries in children and the frequency of conjunctival haemorrhage in newborn infants.

The striking parallelism of the four curves suggests that the seasonal variation in the frequency of haemorrhagic tendency in the newborn infant is linked with the seasonal variation in the fragility of the capillaries. In other words, on the basis of the parallelism of the four curves, we feel that in winter and spring a greater number of infants are born with fragile capillaries than in summer and autumn; accordingly a trauma of constant intensity will result in a higher incidence of birth haemorrhages in the former seasons.



A contributory cause to this peculiar seasonal incidence of birth injury seems to be the prothrombin deficiency occurring, as has been said, with greater frequency in those seasons when capillary resistance is at its lowest. The parallelism in the seasonal decrease in prothrombin level and in capillary resistance is suggestive of a simultaneous deficiency both of vitamin K and vitamin P in the maternal diet in winter and spring.

Capillary Permeability

The striking seasonal fluctuation in capillary fragility, described above, suggested the extension of our studies to the examination of seasonal variation in capillary permeability.

The method of Landis' et al. (1932) was used for testing the permeability. A positive pressure of 40 mm. Hg. was applied for thirty minutes to one arm, and blood was then drawn from the veins of both arms. The difference in haematocrit readings or red cell counts of the blood taken from both arms permits the calculation of the amount of fluid escaping from the compressed arm. Under these experimental conditions the amount of this fluid should normally never exceed 6 ml. (Landis et al., 1932; Eppinger, 1935; Armentano, 1940; Gömöri et al., 1947).

In sixty cases of both fragile and resistant capillaries normal capillary permeability was found. The amount of the fluid reached 6 ml. in only two instances; in the remaining fifty-eight cases it was less than 3 ml. The fluid contained no proteins.

This negative result suggested the examination of capillary fragility in cases showing pathological increase of capillary permeability. This comparative study of permeability and fragility was carried out on four infants suffering from intestinal toxicosis. The figures are demonstrated in table 2.

The data show that even a considerable increase in permeability may occur without any influence on resistance. This lack of parallelism between pathologic permeability and fragility of the capillaries suggests that the underlying cause for the pathologic changes in increased permeability and increased fragility is different. In the origin of increased fragility lack of vitamin P (Armentano et al., 1936; Rusznyák and Szent-Györgyi, 1936; Zacho, 1939; Scarborough, 1940; Rapaport, 1941; Bicknell and Prescott, 1946) has been described as of outstanding importance. Less is known about increased permeability. It seems that toxic or bacterial damage to the capillaries results in the increase of their permeability (Kerpel-Fronius, 1947). A detailed

TABLE 2
CAPILLARY PERMEABILITY AND FRAGILITY

Diagnosis	Amount of escaped fluid (ml.)	Protein content of escaped fluid (per cent.)	Borbély's Test (Hg. cm.)	Rumpel-Leede
Toxicosis	19	5·37	20	—
Toxicosis	18	not determined	20	—
Toxicosis	22	4·5	25	—
Toxicosis	20	not determined	25	—

discussion of the latter problem, however, is not the purpose of this paper.

Summary and Conclusions

Capillary fragility shows a decided seasonal variation, while capillary permeability is not influenced by the seasons.

The higher frequency of cephalhaematomata and cerebral haemorrhage in winter and spring seems to be linked with a parallel seasonal variation in capillary fragility and prothrombin deficiency. The parallelism in the seasonal decrease in prothrombin level and in capillary resistance suggests a simultaneous deficiency of both vitamins K and P in the maternal diet during winter and spring. As a prophylactic measure, therefore, it is suggested that vitamins K and P should be given simultaneously during the last months of pregnancy.

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AN EPIDEMIC OF GLANDULAR FEVER

BY

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An outbreak of lymphadenitis with fever, presenting several features of interest, occurred at a boys' preparatory boarding school during the summer term, 1947. The school is situated in the country, and laboratory facilities are not readily available. Investigations were therefore started late and are not complete, so conclusions must be regarded as tentative.

The Outbreak

In May, 1947, one of the boys became ill with fever, a sore throat, and enlargement of the parotid and cervical glands, giving him the appearance of having mumps, a diagnosis which was at first suggested. A week later a second boy became ill with similar signs and symptoms, including enlargement of the parotid gland on both sides. It was then found that both boys had had mumps a year previously while at the same school and the diagnosis became suspect.

During the few days succeeding the onset of the second boy's illness, five more boys developed enlarged cervical glands with sore throats and fever. The parotid glands in these cases were not enlarged. Palpable glands were also found in the axillae or groins or both. In no case was the spleen enlarged. Temperatures ranged from 99° to 102° F. The boys were isolated in a dormitory and a preliminary diagnosis of glandular fever was made. Laboratory investigations were commenced at this stage, throat swabs were examined, and differential white counts and Paul Bunnel reactions were carried out.

During the next week, ten more boys were admitted with enlarged glands and a slight temperature. It was therefore decided to examine the remainder of the boys in the school, and it was found that another twenty-one (bringing the total to thirty-eight out of eighty-one) had enlarged cervical glands, and many of them also had enlarged axillary glands, and had at some time felt a little 'off colour,' having had a slight sore throat or stiff neck, but had not felt sufficiently ill to report sick. Two of these boys had a temperature of 99° F. when examined and were taken into the sick room. Three more cases occurred at a later date.

It is interesting to note that each succeeding batch of boys was less severely affected than the preceding batch. The early and most severe cases took from eight to ten weeks to recover, as shown by loss of fever, diminishing glandular enlargements, and the return to normal of the blood count, whereas the majority of the later cases were absent from school for periods of from three to ten days, and some not at all. Blood counts were not carried out in the milder cases. The disease had completely died out by the end of July.

Clinical Picture

Glandular enlargement. In the first two cases, both parotid glands were grossly swollen, the tonsillar glands were as large as walnuts, and the glands in the posterior triangles were palpable, as were the glands in the axillae and groin. The parotid swelling subsided in about ten days, but the tonsillar and other cervical glands subsided very slowly, gradually diminishing over a period of from eight to ten weeks. In the second group the tonsillar glands were the most enlarged, but other glands were palpable in the neck and axillae. The glands in the neck were often tender and caused the

TABLE 1

DIFFERENTIAL WHITE COUNT, PAUL BUNNEL, AND THROAT SWAB RESULTS

Case	Lymphocytes %	Polymorphs %	Monocytes %	Eosinophils %	Paul Bunnel	Week of illness	Throat swabs	
							Streptococci	Vincent's organism
1	34	54	4	7	neg.	Second	+	neg.
2	31	64	3	2	neg.	Second	+	neg.
3	29	43	11	7	neg.	First	neg.	neg.
4	28	57	8	7	neg.	First	neg.	neg.
5	33	52	12	3	neg.	First	+	neg.
6	31	62	7	nil	neg.	First	neg.	neg.
7	11	64	11	9	neg.	First	neg.	neg.

TABLE 2
LATER BLOOD COUNTS ON CASES 2, 5, 6, AND 7

Case	Total white	Lymphocytes		Polymorphs		Monocytes		Eosinophils		Red count (millions per c.mm.)	Hb. %	Week of illness
		%	Total	%	Total	%	Total	%	Total			
2	21,700	6	1,302	85	18,445	3	651	6	1,302	3·7	64	4th
5	10,800	30	3,240	48	5,184	7	756	15	1,602	4·2	80	5th
6	6,400	27	1,720	36	2,304	14	896	22	1,408	3·65	66	5th
7	9,000	19	1,786	44	4,176	4	376	31	2,914	4·37	70	13th

neck to ache. In the later cases a few palpable glands with or without a slight pyrexia were all that was found on clinical examination. It was noticed that the left side of the body was more commonly involved than the right.

Temperature. In the first two cases the temperature ranged from 100° F. to 102° F. while the glandular enlargement was at its height and subsided with the parotid enlargement. In other cases the degree of pyrexia varied in relation to the size of the glands, and in cases where glands were only just palpable was normal, or only slightly raised.

Investigations

These were commenced as soon as glandular fever was suspected. In table 1 the differential white count, Paul Bunnel, and throat swab results are shown. It will be seen that there was only a slight, and in some cases no, increase in mononuclear cells; on the other hand there was a very definite eosinophilia in five out of seven cases. The Paul Bunnel titrations were within normal limits, and the throat swabs were inconclusive. It was therefore decided to repeat some of the blood counts and Paul Bunnel tests at a later date. This was done in cases where the eosinophilia was lowest, and the results are shown in table 2. The total white counts were estimated on this occasion and varied considerably; the high count in Case 2 can probably be accounted for by the streptococcal throat infection which complicated this case. The striking point was the marked eosinophilia, the total eosinophil count being about the same in each case. It can be seen that the eosinophil count increased, as the illness progressed, well into convalescence. There was also a secondary anaemia. The Paul Bunnel reactions remained negative in Cases 2, 5, and 6 and was not repeated in Case 7. In Cases 2, 5, and 6 stools were examined for worms and ova when eosinophilia was at its height, and intradermal tests were done to exclude trichiniasis. The results were negative.

Discussion

A number of interesting facts came to light during this epidemic, which was presumably one of glandular fever. Glandular fever is described in many different forms, varying in adults and in children. In children, where epidemics are usually seen, variations are extremely common. In certain cases blood counts may even be normal (Whitby and Britten, 1942).

The most difficult task at the beginning was to make a diagnosis. The first two cases resembled mumps; the next five cases suggested glandular fever, but the laboratory findings did not confirm this, since the Paul Bunnel tests were negative, and the increase in mononuclear cells small, while that of eosinophils was comparatively great. There was no splenic enlargement (Bernstein, 1940, reports splenic enlargement in 50 per cent. of cases, as do other writers).

At first it was considered that this might be a new disease characterized by lymphadenitis with eosinophilia, possibly due to a virus or other infection, to be associated with (i) infectious mononucleosis, (ii) infectious lymphocytosis.

Further investigations, although limited, showed that:

1. The Paul Bunnel was still negative after five to six weeks from the onset in the three cases in which it was repeated. Some writers state that the Paul Bunnel test is positive in almost 100 per cent. of cases. In a series of seventy-eight, Kaufman (1944) found that 75 per cent. gave a positive reaction at varying stages. Paul (1939) and Fuller (1941) both state that a positive reaction may not develop at all. Whitby and Britten (1942) state that in their opinion there are a number of closely related viruses which give rise to the symptom complex, and whilst most of these induce serological changes associated with the Paul Bunnel test, others do not. Himsworth (1941) states that the titre may be influenced by the absolute number of monocytes. This epidemic supports his statement.

2. The eosinophilia which was present in the acute stage, and was a marked feature of this epidemic, increased as the glands slowly subsided, reaching in one case an absolute total of 2,914 and a percentage of 31. A slight eosinophilia has been described in convalescent cases of glandular fever

(Tidy, 1943) and other acute fevers, but it is felt that its appearance was abnormally early, and the ultimate figure comparatively high. No other cause for eosinophilia was discovered.

3. There was a marked secondary anaemia which responded to iron.

Summary

An epidemic of glandular fever has been described occurring in a closed community. The first two cases were severe and showed parotid involvement; the succeeding cases were less severe, and the epidemic died out in three months.

There was only a slight mononucleosis in the first weeks of the disease, which rapidly disappeared. An eosinophilia appeared early and gradually increased for a period up to three months. There was a secondary anaemia. All Paul Bunnel titrations were negative. There was no splenic enlargement.

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THE PLACE OF ORAL PENICILLIN IN PAEDIATRICS

BY

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In the treatment of sick children the disadvantages of a drug which can be administered only by injection are serious. This applies particularly to wasted infants in the throes of a severe infection. Here the minimum of handling is almost as important as the drug.

In February, 1947, it was decided to start an investigation at the Children's Hospital, Birmingham, to determine the reliability of penicillin given by mouth in infancy. Two papers had already appeared in this country. Henderson and McAdam (1946) recorded the results of this method of administration to thirty-seven infants. However, only nine of them were over one month old. When a dose of 10,000 units was used, bacteriostatic serum levels persisted as long as six hours, while 100,000 units produced a serum concentration persisting as long as fifteen hours. Buchanan (1946) determined the results of administering a dose of 4,000 units per pound of expected body weight per day divided up so that it could be administered before feeds. Satisfactory results were claimed in the twenty-five infants investigated, but again they were mostly under the age of one month. Further work at the same school has shown that it is only in premature infants and in the first month of life that consistently reliable serum levels can be obtained with this dose (Guthrie and Montgomery, 1947).

During the course of this work, several publications have appeared. Husson (1947) has investigated the serum levels in twenty-two infants up to the age of five months following a dose of 20,000 units orally. In every case he was able to demonstrate a serum level of at least 0·06 units after an interval of three hours. Suchett-Kaye and Latter (1947) treated twenty-five children suffering from pneumonia with oral penicillin. Their ages ranged from three months to two years. The doses used varied from 10,000 to 40,000 units at three- to four-hourly intervals. In only six of the thirteen estimations performed at three hours after the dose was a bacteriostatic level recorded. Despite this, good clinical results were obtained in all but the four most seriously ill cases. One of these was infected with a penicillin-resistant organism. Hoffman et al. (1948) have performed an extensive survey of this problem in children from infancy up to the age of twelve years. Forty-two infants up to the age of one year suffering from respiratory-tract infections were treated with oral doses of 20,000 units three-hourly. In six of them no level was recorded at an interval of three hours, and in five it was only 0·03 unit. The problem has been tackled in older children, but all workers agree that the results obtained are less reliable and the serum levels less sustained than in infancy even with the use of massive doses. Markowitz and Kuttner (1947) gave 50,000 units before breakfast to twenty children up to the age of twelve years. The serum levels in no case persisted longer than two hours. Further, there was an unaccountable variation in the levels obtained in the same individual on successive days with the same dose. Reisman et al. (1947), using a dose of 100,000 units, did not obtain any better result. A case of bacterial endocarditis responding to oral penicillin has been recorded (Burke et al., 1946). This was a girl of eleven years who received 100,000 units three-hourly for fourteen days.

There is complete uniformity of opinion that the drug should be given on an empty stomach in order to ensure maximum absorption. The use of buffered solutions now receives little support. Stewart and May (1947) show that an aqueous unbuffered solution gives the best result. Further, their investigations demonstrate that unless the pH of the gastric secretion falls below a level of 3, it exerts no destructive action on penicillin. They also found that in some cases the administration of glucose with the drug increased the maintenance of the serum level.

Method of Assay

The best results were obtained using the micro-method described by Fleming and Smith (1947). Human plasma was found more satisfactory than horse serum in making up the ' His Serum water ' since it was less liable to become turbid following sterilization. Phenol red was used as indicator and gave the best end point. As test organism the Oxford strain of Staphylococcus aureus 209 was employed. It showed a complete inhibition of growth in a concentration of 0·0135 I.U. per ml.

British standard penicillin supplied by the National Institute for Medical Research. Since some of the cases received sulphonamides as well as oral penicillin, it was necessary to determine the sensitivity of the organism to this group of drugs. Addition of sulphadiazine to a human serum containing penicillin up to a maximal concentration of 16 mg. per 100 ml. did not affect the estimation of the penicillin concentration. Controls were also performed by adding para-aminobenzoic acid in one or two cases where the babies were receiving both drugs. In no case was there any significant alteration in the reading obtained. It was concluded that with this strain of organism the presence of sulphonamides could be ignored.

Investigation of Absorption

The absorption of penicillin from the alimentary tract of forty infants has been investigated and sixty-three serial estimations of serum penicillin levels undertaken. The first experiment consisted in giving a single large dose and watching the fate of the penicillin in the serum at hourly intervals. In some cases a similar dose was injected on the following day for comparison. The results are set out in table 1. For a period of three hours the levels following injection are very much higher than those after oral administration. Subsequently, if the levels are observed over a further period of five hours, there is little to choose between the two methods.

The next problem was to find a method of oral administration which would ensure a sustained level sufficient to deal with virulent infections by penicillin-sensitive organisms. Instructions were given that penicillin in aqueous solution of a strength of 20,000 units per ml. should be administered in ¼ to ½ oz. of the feed by spoon immediately before the feed. There was very little difficulty in persuading the majority of babies to take the drug. The addition of a little sugar sometimes helped. There is an element of chance about the administration of any drug by mouth to a small baby, and this is reflected in a few of the results. They are recorded in table 2.

In the first six cases small doses were used as advocated by previous workers. It was considered that a sustained level of not less than 0·04 units per ml. was advisable to deal with severe infections. By this standard these doses are clearly inadequate. In two cases, 2 and 5, the effect of giving between three and four times the dose was tried. Excellent sustained levels were obtained. Since both these babies were under two months old, it was decided to try giving proportionately large doses to older ones. Up to the age of six months satisfactory absorption from the intestinal tract was recorded in twenty-seven babies with three exceptions. Case 7 received too small a dose. It was learned subsequently that the age and not the weight of the baby should be the guiding factor. Case 15 was suffering from a very severe attack of enteritis; the stools were watery and offensive, and contained some

TABLE 1

A COMPARISON OF ORAL AND INTRAMUSCULAR ADMINISTRATION

No.	Age	Weight (lb.)	Dose	Hourly serum levels (units per ml.)								Remarks
				1	2	3	4	5	6	7	8	
1	5 m.	14¾	Oral 100,000	0·16	0·16	0·16	0·08	0·04	0·04	0·03	0	
			I.M.	1·20	1·20	0·32	0·08	0·03	0·03	0		
2	2 m.	10	Oral 100,000	0·08	0·32	0·64	0·32	0·16	0·04	0·03	0	
			I.M.	2·50	1·20	1·20	0·64	0·16	0·16	0·08		
3	3 wk.	7½	Oral 7,000	0	0·04	0·04	0·04	0·03	0·03	0·03	0·03	
			Oral 50,000	0·64	0·32	0·32	0·64	0·64	0·64	0·16	0·32	
			I.M.	M	M	1·20	0·64	0·64	0·32	0·16	0·08	
4	3 wk.		Oral 100,000	0·32	0·64	0·32	0·16	0·04	0	0		
			I.M.	M	M	M	0·64	0·08	0·04	0·04		
5	5 m.	9½	Oral 100,000	0·32	0·64	0·08	0·08	0·04	0·04	0·03	0	
6	9 m.	12	Oral 100,000	0·64	0·32	0·32	0·04	0·03	0·03	0·03	0	Mixed feeding
			I.M.	2·50	0·64	0·16	0·08	0·04	0·03	0·03	0	
7	2½ m.	7	Oral 50,000	0·08	0·08	0·08	0·08	0·04	0·04			Pyloric stenosis

M indicates a level of over 1·2 units per ml.

TABLE 2
SERUM LEVELS OBTAINED IN CASES RECEIVING ORAL PENICILLIN AT REGULAR INTERVALS

	No.	Age	Weight (lb.)	Dose	Hourly serum levels (units per ml.)						Remarks
					1	2	3	4	5	6	
Cases receiving small doses	1	2½ m.	6½	5,000 3-hourly	0	0	0				Premature
	2	1½ m.	6½	7,000 3-hourly	0·04	0·03	0	0·03	0·03	0·03	
	3	1½ m.	6	5,000 3-hourly	0·04	0·04	0·04	0·03	0·03	0·04	
	4	2 m.	4½	7,000 4-hourly	0·04	0·04	0·03	0			Premature
	5	1 wk.	6¾	5,000 3-hourly	0·04	0·04	0·04	0·04	0·03		
	6	2 m.	8	10,000 3-hourly	0·03	0·04	0·03				
Cases receiving moderate doses	7	2½ m.	5½	20,000 3-hourly	0·04	0·04	0·03	0	0·03	0·03	Premature
	8	2½ m.	7¾	20,000 4-hourly	0	0·08	0·16	0	0·32	0·04	
	9	3 m.		20,000 3-hourly	0·16	0·32	0·16				Nephrosis
	10	1 m.	6	20,000 3-hourly	0·64 0·32	0·32 0·32	0·16 0·32				
	(2)	1½ m.	6½	20,000 3-hourly	0·16	0·16	0·32	0·32	0·16	0·32	
	(5)	1 wk.	6¾	20,000 3-hourly	0·08	0·16	0·16				
Cases receiving large doses	11	1½ m.	7	30,000 4-hourly	0·16	0·32	0·32	0·08	0·08	0·04	
	12	2½ m.	7	40,000 3-hourly	0·16	0·16	0·08	0·08	0·16	0·32	
	13	1½ m.	5½	40,000 3-hourly	0·08	0·08	0·16	0·32	0·64	1·2	Premature
	14	4 m.	10½	40,000 3-hourly	0·64	0·64	0·64	0·32	0·64	0·64	
	15	2 m.	8½	40,000 3-hourly	0	0·03	0·03	0	0·03	0·03	Severe enteritis
	16	3 m.	11	50,000 3-hourly	0·08	0·08	0·08	0·16	0·16	0·08	
	17	5 m.	9½	50,000 3-hourly	0·32	0·16	0·08	0·64	0·32	0·16	
	18	4½ m.	9½	50,000 3-hourly	0·03 0·32	0·04 0·32	0·08 0·32	1·2	1·2	M	
	19	3 m.	7½	50,000 3-hourly	0·64	0·64	0·32				
	20	2 m.	8¾	60,000 4-hourly	No level attained						Pyloric stenosis
	21	4 m.		60,000 3-hourly	0·03	0·04	0·04				
	22	3 m.	10¾	60,000 4-hourly	0·64	0·32	0·16	0·16	0·64	0·64	
	23	3 m.	11	60,000 4-hourly	0·64	0·64	0·32	0·04			
	24	2 m.	8½	60,000 6-hourly	0·03 0·04	0·03 0·04	0·04 0·08	0·04 0·04	0·04 0·04	0·04 0·04	
	25	3 m.	10¾	70,000 4-hourly	1·2	0·64	0·32	0·32			
	26	4 m.	10½	70,000 4-hourly	0·32 0·64	0·64 1·2	0·32 0·64	0·16 0·32	0·16	0·64	
	(2)	5½ m.	7	70,000 4-hourly	0·16	0·16	0·16	0·16			
	27	6 m.	13¾	70,000 4-hourly	0·32	0·16	0·16	0·08			
	28	5 m.	12½	70,000 3-hourly 4-hourly	0·03 0	0 0	0·08 0·16	0·32 0·08	0·16		
	29	3 m.	5½	80,000 4-hourly	All levels over 1·2						
	30	4 m.		80,000 3-hourly	0·08	0·16	0·04	0·16	0·08	0·08	
Cases over 6 months on mixed diet	(30)	5½ m.	13	70,000 4-hourly	0	0	0·03	0·03	0		
	31	7½ m.	16½	70,000 4-hourly	0·03	0	0·03				
				100,000 4-hourly	0	0·03	0·16	0·16			
	(17)	7 m.		100,000 4-hourly	0·03	0·04	0·03	0·03			
	32	7 m.	16	100,000 4-hourly	0·16	0·04	0				
	33	8 m.	14	100,000 3-hourly	0·04	0·04	0·04	0·04	0·04	0·04	

Where the case number is enclosed in brackets, this indicates that previous investigations have been carried out on the same baby and are recorded earlier in the table.
M indicates a level of over 1·2 units per ml.

blood and mucus. Several of the other babies had relaxed, undigested stools caused by food intolerance consequent on some infection outside the alimentary tract, and yet absorbed the drug well. Case 20 suffered from pyloric stenosis with frequent vomiting. The wide variations in the levels in Cases 18 and 28 almost certainly reflect a failure in the technique of administration.

It was observed that the addition of cereals to the diet sometimes coincided with a diminution in the efficiency of the absorption of penicillin from the alimentary tract. Two cases, 17 and 30, originally absorbed the drug well, but after an interval of six weeks, during which cereals had been started, a further test was made. The falling off in absorption was definite. In all, five cases on a mixed diet were investigated. Even a dose of 100,000 units was not sufficient to ensure an adequate serum level. It is not known if there is any real connexion between these two factors, nor can any explanation be advanced. Incubation of a solution of penicillin with a suspension of a cereal food for several hours in the laboratory failed to demonstrate any adsorption of the drug.

TABLE 3

DOSES OF PENICILLIN BY MOUTH

Age	3-hourly	4-hourly
0-6 weeks	.. 20,000 U	30,000 U
6 weeks-3 months	.. 40,000 U	60,000 U
3 months-6 months	.. 50,000 U	70,000 U

Case 9, a three-month-old baby suffering from the nephrotic syndrome, was of interest. It demonstrated the excellent levels which may be obtained in these cases with moderate dosage. A similar result was obtained in a boy of two and a half years suffering from the same disease. Immaturity of the infant kidney is believed to contribute to the success achieved with oral penicillin in the early months of life.

The absorption of the drug from the alimentary tract of one or two older children was observed, using a dose of 100,000 units. The results were so unreliable that the investigation was abandoned.

As a result of this work it is claimed that penicillin may be administered orally to any infant below the age of six months as reliably as the sulphonamides, provided a big enough dose is employed and mixed feeding has not been started. It is not agreed that injection is the route of choice in severely ill babies. It is just in these cases that the full advantages of oral administration are apparent. Where there is persistent vomiting or severe enteritis parenteral administration must be employed. The relaxed undigested stools so frequently seen in the course of infection in infancy are not a contraindication to giving the drug by mouth. Further, it was found that the modification of the feed by lactic acid does not destroy the penicillin.

The size of the dose must be based on the age and not the weight of the infant. This rule applies to premature babies as well. Table 3 shows the doses employed at this hospital. These doses are given immediately before each feed. At night a double dose is given before the last feed.

Using these doses, success has been achieved not only in treating respiratory tract infection, but also in at least one case of multiple osteomyelitis which had failed to respond to the sulphonamides. In no case have any toxic manifestations been observed.

Claims have been made that oral penicillin used in the same dose as intramuscular administration will attain as good a level in infancy. Examination of the levels in some half-dozen babies under treatment with intramuscular penicillin, selected at random from different wards, shows that this is not true. These results are recorded in table 4.

TABLE 4

BLOOD LEVELS DURING ROUTINE INTRA-MUSCULAR ADMINISTRATION

No.	Age (months)	Weight (lb.)	Dose	Hourly levels (units per ml.)							
				1	2	3	4	5	6	7	8
1	3	9	20,000 3-hourly	0·04	0·03	0·03	0·04				
2	9	17	10,000 3-hourly	0·16	0·16	0·64	0·16	0·04	0·03		
3	4	11	20,000 4-hourly	0·16	0·08	0·08	0·08	0·08	0·16	0·16	0·16
4	7	13½	30,000 3-hourly	M	0·32	M	M	0·32	0·16		
5	2½	8½	12,000 3-hourly	0·04	0·32	0·16	M	0·64			
6	7	15	30,000 3-hourly	0·64	0·32	0·16	1·2	0·32	0·16		

M indicates a level of over 1·2 units per ml.

Summary

Oral administration of penicillin is the method of choice up to the age of six months.

It is not suitable when there is severe enteritis or persistent vomiting.

Owing to the unpredictable variation in absorption, it is essential to use massive doses.

In older children the success of oral administration becomes a matter of trial and error. It is certainly to be condemned in cases of severe illness.

My thanks are due to Miss S. Baar for her tireless work in carrying out the penicillin assays and to Dr. H. S. Baar for his criticism and advice.

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AMINO ACIDS IN THE FEEDING OF INFANTS*

BY

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Introduction

Enzymic digests of protein, which only became available in this country during the later years of the war, had been made use of in the U.S.A. and Sweden for some time before then. The preparations which we have been using are digests of the casein of cows' milk. All such preparations have a bitter and unpleasant taste due to the presence of free amino acids, although this can be modified to some extent by dilution with milk. Fortunately this disadvantage does not constitute any serious drawback to their employment in infants up to three months of age, who do not appear to resent this taste, and this is the age group in which such pre-digested proteins have a great field of usefulness.

Indications for Amino Acid Feeds

There are obvious advantages in feeding pre-digested rather than raw protein to cases of cystic fibrosis of the pancreas whose duodenal secretions are deficient or completely lacking in trypsin. It has recently been demonstrated (West et al., 1946) that the level of plasma amino acid nitrogen rises in these cases after a meal of hydrolysed casein, indicating absorption from the gut, but not after a meal of unhydrolysed casein or gelatin. This difference is not shown by infants with a normal pancreas. Clearly, the absorption of protein by patients with pancreatic insufficiency is improved by feeding hydrolysed protein.

For those infants who manifest an allergic reaction to the proteins of cows' milk, it would seem reasonable to reduce the protein to its constituent amino acids before administration in an attempt to obviate the adverse effects of ingesting raw protein. This has, in fact, been tried with success (Hill, 1941).

There are two large groups of patients in whom oral fluids are contraindicated, namely those suffering from congenital or acquired obstruction of the alimentary tract, and those suffering from gastro-enteritis of severe degree. In such cases the daily basal protein requirements must be administered parenterally. In these circumstances protein hydrolysates have proved invaluable, since, apart from the use of human plasma and blood, only protein in the form of amino acids may be given parenterally with safety.

The mixture of polypeptides and amino acids in these enzymic digests does not form a curd in the stomach, and is easily absorbed by the alimentary tract without need for much digestive activity. Hence hydrolysed casein is a valuable source of protein for any infant who cannot tolerate his full protein requirement as unmodified milk protein but who can take oral fluids. Such relative intolerance may be due to increased protein requirements or alimentary insufficiency. Often both factors occur together in the same individual.

In acute infections there is an increased need for protein but there is also a diminished tolerance for food by the gastro-intestinal tract, whether the infection is of enteral or parenteral origin. Here, too, pre-digested protein is a beneficial therapeutic adjunct.

Wasted infants require a high protein intake to make good their depletion of body protein. Whether this has come about as a result of pure starvation, as in pyloric stenosis, or as the result of infection, full milk feeds must be introduced with caution if vomiting and diarrhoea are to be avoided. In view of the diminished digestive powers of these infants (Andersen, 1942; Miller, 1941) protein digests fulfil a valuable function.

Premature infants at birth have a lower nitrogen content per kilo of body weight than full-term infants, and therefore require a high protein intake to make good this deficit and maintain growth. It has been shown that the enzymic activity of the stomach and bowel tends to be low (Miller, 1941), especially in the less mature and smaller infants, and therefore their protein must be supplied to them in a form that their digestive tracts can readily assimilate.

The indications for amino acid feeding may be

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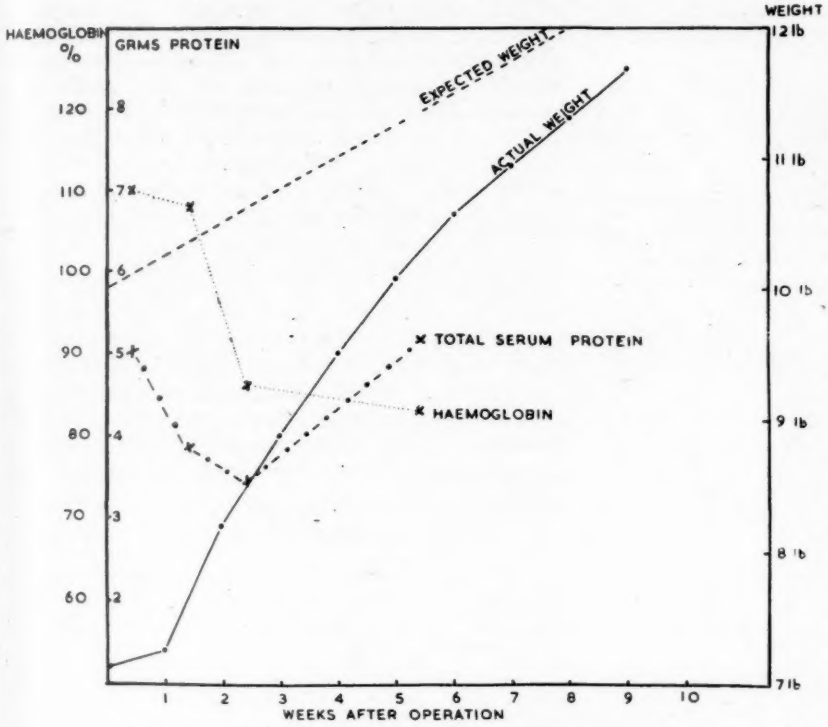

FIG. 1.—A case of pyloric stenosis aged four weeks, 7 per cent. of the expected weight at operation.

listed as follows: (1) cystic fibrosis of the pancreas; (2) milk protein allergy; (3) parenteral feeding; (4) acute enteral or parenteral infection; (5) marasmus; (6) prematurity.

Investigation in Birmingham

At the time when British enzymic digests of casein were first made available by the Medical Research Council, Shohl and his co-workers (1939) had already published the results of feeding experiments with the American preparation, Amigen (Mead Johnson) and had shown by balance experiments that the nitrogen in this preparation is equal to that in evaporated milk in promoting nitrogen retention in normal infants. Furthermore, Magnusson (1944) had published a preliminary report on the value of a Swedish preparation, Aminosol, as a supplement to human milk for premature infants.

In view of these reports it was decided to embark on an investigation of the value of protein digests in certain groups of patients, particularly marasmic and premature infants.

A. **Marasmic infants.** During recent years, knowledge of the protein metabolism of man and animals has been greatly extended and the severe degree of protein depletion which exists in chronically wasted individuals appreciated. A high protein as well as a high caloric intake is required if repair and recovery is to proceed smoothly and at a maximum rate. Limits to the achievement of this aim are often set by anorexia and intolerance of food, and it is in these circumstances that protein hydrolysates have proved advantageous.

The term 'marasmus' may be defined as indicating that an infant is under 80 per cent. of his expected weight, based on age and birth weight.

The feed used has been a dilute lactic acid milk with the addition of dextrimaltose and 2·2 per cent. of amino acids (Young et al., in the press). This contains 3·9 per cent. protein, a calorie value of 20 per oz. and provides about 6·5 g. of protein per kg. daily —or just under 3 g. per lb. It is well tolerated.

The accepted criteria for assessing protein nutrition in the infant are maintenance of: (1) normal weight gain; (2) positive nitrogen balance; and (3) normal amounts blood proteins especially serum albumin. Restoration of these values may be taken as an indication of successful treatment of protein depletion. We have been able to measure only (1) and (3) in the infants we have studied.

A comparison has been made of the postoperative average weekly weight gains in a small series of uncomplicated cases of pyloric stenosis and associated marasmus fed on breast milk with an equal number of similar cases fed on the above mentioned high-protein feeds. The weight gains were practically identical in the two series. Since the feeds are both equal to 20 calories per oz. the average caloric intake in the two groups is the same in each week. It is reasonable to presume, therefore, that the optimal weight gains in these artificially fed babies is due to the additional protein intake.

Changes in the amounts of haemoglobin and plasma proteins are liable, when estimated by the concentration of these proteins in the blood, to be masked by changes in blood volume. During the stage of regeneration after protein depletion, blood volume, haemoglobin, and plasma proteins are all increasing in amount; but the former regains its normal level at a more rapid rate, resulting in a temporary haemodilution with apparent increase in the anaemia and hypoproteinaemia. This has been proved by specially designed experimental investigations to occur in both man and animals (Walters et al., 1947; Weech et al., 1937).

Preliminary investigations show that the same mechanism is operative in the regenerative phase of infantile marasmus.

Fig. 1 shows the postoperative course of an uncomplicated case of pyloric stenosis who was 71 per cent. of his expected weight at the start of treatment.

B. Premature infants. A reasonable assumption is that the optimum weight gain for a premature infant in the first few months of life is the rate at which it would be gaining in utero had pregnancy continued to term. Table 1 is adapted from Huggett (1946), and shows the average daily deposition of protein by the foetus. Taken in conjunction with the average weights of foetuses of various ages, these figures represent a deposition of about 1 g. per lb. body weight daily. Assuming a protein content of 1·5 per cent. in human milk and a utilization of 50 per cent., a daily intake of 4¾ oz. of breast milk per lb. of body weight would be necessary to supply the quantity of protein required.

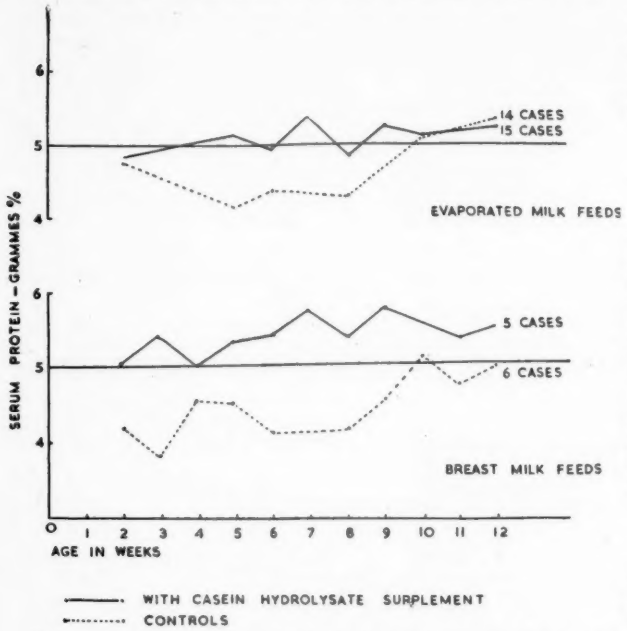

FIG. 2.—Total serum protein in forty premature infants.

TABLE 1

AVERAGE DAILY DEPOSITION OF PROTEIN BY THE FOETUS (HUGGETT)

Stage of foetal life	Protein deposition
Throughout foetal life	1·4 g.
In last three lunar months ..	3·57 g.
In last month	6·4 g.

This rate of growth represents the optimum weight gain, but a slower rate seems to be compatible with good physical and mental development. Weight gains comparable to those in utero have, however, been achieved by Jorpes et al. (1946) who added 2·5 g. casein hydrolysate per kilo body weight per day to breast milk, and by Lind (1945) who added 1·5 g. protein as dried human plasma per kilo body weight per day to breast milk.

In our investigation (Young et al., in the press) we have used four feeds. Two of these are based on breast milk and two on an evaporated cow's milk mixture. The two breast milk feeds have the same caloric value, but in one the protein content is brought up to 3·5 per cent. by the addition of 2·2 per cent. amino acids, and in the other the protein content is only 1·5 per cent. Similarly, the evaporated milk mixtures are equicaloric, but the protein contents are 3·8 per cent. and 1·6 per cent. (table 2).

TABLE 2

COMPOSITION OF FEEDS

	Protein %	Fat %	Carbohyd. %	Cals. %
Evaporated milk mixture (control)	1·6	1·9	9·2	17·5
Evaporated milk mixture with casein hydrolysate	3·8 (1·6 milk + 2·2 cas. hyd.)	1·9	7·0	17·5
Breast milk (control)	1·5	3·3-4·0	7·5	19-20
Breast milk with casein hydrolysate	3·5 (1·3 milk + 2·2 cas. hyd.)	2·9	6·6	20

All observers agree that the total serum protein concentration in the premature infant at birth is lower than that in the full-term infant; the average value is under 5 g. per cent. Fig. 2 shows the average levels of serum protein, in two groups of premature infants fed on unmodified breast milk and breast milk with added protein, the daily protein intake being approximately 1·5 g. per lb. in the first and 2·5 g. per lb. in the second: and another two similar groups fed on evaporated milk with high and low protein content. The higher serum protein levels achieved with the additional hydrolysed protein is clearly shown in both groups.

C. Parenteral administration. Using a solution of hydrolysed casein; Shohl (1943) found that 2·2 g. of protein per kg. body weight (1 g. per lb.) daily is required to keep an infant in nitrogen balance. This may be accepted as the minimum daily requirement. Amounts in excess of this may be utilized as a source of energy and not of protein when the total caloric intake is low, as is inevitably so with parenteral alimentation alone.

We have favoured solutions of strengths of 1·7 per cent. and 2·5 per cent. casein hydrolysate, with 5 per cent. glucose. This is given by slow intravenous drip. No untoward reactions during

administration have been encountered. The flushing, pyrexia, and vomiting observed by earlier workers may have been due to impurities in the preparation, which have been eliminated by improved methods of manufacture.

Conclusion

Our observations on this mode of therapy are at the present stage limited to clinical impressions. Briefly, it has been demonstrated to be a valuable additional aid in the management of congenital abnormalities of the gut. A bolder policy is possible in the treatment of gastro-enteritis; and complete deprivation of oral feeds in young infants is a much less hazardous step. There is a noticeable diminution in the intractable anorexia (probably due to specific amino-acid deficiency) so often a major problem in the treatment of gastro-enteritis. Gross fatty changes in the liver are not so frequently seen in those who fail to survive.

I am indebted for their help to Drs. Y. J. Williams and P. Poyner-Wall, the latter of whom is in receipt of a grant from the Medical Research Council. The expenses of the laboratory work were defrayed by a grant from Messrs. Cow and Gate, Ltd.

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SEPTICAEMIA OF THE NEWBORN

A CLINICAL STUDY OF FIFTEEN CASES

BY

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Analysis of the causes of death in the neonatal period shows that infection is frequently responsible. In different series (Cruickshank, 1930; d'Esopo and Marchetti, 1942; Parsons, 1944; Macgregor, 1946; Scottish Scientific Advisory Committee, 1947) the incidence has varied between 8 per cent. and 42 per cent. The incidence of infective conditions in the neonatal period, other than those causing death, is also high. Corner (1946) reported 6,534 consecutive live births in two maternity units in Bristol, and found that 25·3 per cent. of all babies in one hospital and 29·7 per cent. in another had evidence of infection.

Recognition of the symptoms and signs of neonatal septicaemia at an early stage, followed by adequate treatment, would greatly reduce neonatal mortality. The object of this paper, dealing with fifteen cases of neonatal septicaemia admitted to the Queen Elizabeth Hospital for Children, London, during 1946, is to point out the paucity of signs and symptoms in the majority of these cases, to stress the difficulty of diagnosis unless routine blood cultures are taken in all obscure illnesses of the newborn, and to describe the results of treatment.

Criteria of Diagnosis

Although the crucial test of the septicaemic nature of an illness is the isolation of the causative organism from the blood stream, there is no reason why a positive blood culture should invariably be required before the diagnosis of septicaemia is made. Strong presumptive evidence of septicaemia may be afforded by osteomyelitis, meningitis, or by multiple abscesses in the subcutaneous or deep tissues.

Etiology and Pathogenesis

The organisms commonly responsible for septicaemia in the newborn are staphylococcus, streptococcus, and B. coli; less frequently pneumococcus, meningococcus, pyocyaneus, proteus, paratyphoid, Gaertner, Klebs-Löffler bacilli, and monilia are encountered. In Dunham's (1933) series of thirty-nine cases, septicaemia was due to streptococcus in fifteen cases, staphylococcus in eleven cases, B. coli in ten, pneumococcus in two, and pyocyaneus in one.

Infection may occur before birth, during delivery, or after birth.

(a) **Before birth.** Clifford (1947) recently reported three cases of maternal septicaemia in which positive blood cultures were obtained from the babies at birth. The organisms were β-haemolytic streptococcus, B. coli, and B. Suipestifer. Laffont and Mele (1926) reported a similar case.

(b) **During delivery.** Browne (1921) stressed the importance of inhalation of bacteria in the production of neonatal infections and stated that B. coli are frequently found in infection of the lungs. Gonorrhoeal ophthalmia and monilia infection may also be acquired during the infant's passage down the birth canal. Dodd (1947) has recently shown that the virus of epidemic diarrhoea of the newborn may be acquired in a similar manner. Infected maternal passages may thus be a potent focus from which organisms are transferred from mother to child.

(c) **After birth.** Obviously there is a risk of transference of organisms to the newly born from the nose, throat, and hands of the attendants, and through infected fluids given by feeding bottles. Entry of the organisms into the baby may occur via skin, umbilicus, mouth, and respiratory tract.

Clinical Features

Fifteen cases of septicaemia are reported, but two do not fall strictly into the neonatal period—their ages being forty-nine days and sixty-seven days on admission; they are included because the symptoms and signs were similar to those of babies admitted during the first four weeks of life. The cases are considered in groups, based upon the probable mode of entry of the organisms into the child's body.

Group A: Umbilical infection. There were six cases in this group, four were male and two female. The umbilicus appeared normal in two cases; in one case the cord was still attached at the age of three weeks and appeared puffy and inflamed; in the remaining three cases the umbilicus was sticky and surrounded by exudate, which in one case was blood-stained. All six cases had frequent fluid

stools, and in three vomiting also occurred. There was marked loss of weight in the absence of dehydration. In four cases the appetite was normal. Haemorrhages occurred in three cases, and jaundice in two. The liver was enlarged in only one case, and in no case was the spleen palpable. Pyrexia over 100° F. occurred in only one case. The white blood counts showed a wide variation, from 10,000 to 31,000 per c.mm., but a high proportion of primitive white cells was present in every case.

Blood culture was successfully undertaken in four cases, and resulted in the isolation of staphylococcus aureus (coagulase positive) in three cases and of staphylococcus albus in one.

Three cases recovered and three died. Post-mortem examinations confirmed the septicaemic nature of the disease process.

The umbilicus of the newborn used to be considered an important portal of entry for organisms capable of producing generalized sepsis (Cullen, 1916; Ritter von Reuss, 1920; Allen, 1930). The older literature describes only the advanced cases of septicaemia, showing jaundice, haemorrhages, and rigors, with obvious local evidence of the source of infection. Friedlaender (1927) showed that local lesions of the umbilicus may be absent, but inflammatory reaction and necrosis of the liver may be present in these cases. Morison (1944) described nine cases of umbilical sepsis and acute interstitial hepatitis.

The common clinical features in my six cases were frequent fluid motions, loss of weight, and primitive white cells in large numbers even when the total white count was normal. Enlargement of the liver and spleen was not observed.

Group B: Skin sepsis. The skin lesions in the three cases in this group were marked. One child had a brawny swelling about three inches in diameter in the left clavicular and pectoral region; the second showed an area of redness and desquamation in the scrotal area which spread rapidly on to the abdominal wall, and the right thigh was swollen as far as the knee; in the third case, multiple septic spots were present on the thigh, legs, buttocks, and scalp; the eyes showed purulent discharge.

Feeds were taken badly in all three cases, and two had frequent, fluid motions. There was loss of weight in two cases. The temperatures were higher than in group A, recordings of 100°, 103°, and 104° F. being obtained. Again no enlargement of liver or spleen was noted. Blood culture was positive in all three cases, staphylococcus aureus (coagulase positive) in two cases, and staphylococcus albus (coagulase positive) in the other case. Two cases died. Castle (1925), Campbell (1931), and Mount (1935) have reported similar cases.

Group C: Respiratory tract. Only two cases in this group were observed, and evidence of septicaemia was not conclusive. One child showed very few clinical signs of respiratory infection, the cry was vigorous, cyanosis was absent, and in the early stages the respiration rate was normal. Fine crepitations were present at both lung bases. In the other child respiratory signs were obvious. There was cyanosis, the respirations were rapid, and pneumonic signs were present in both lungs. In both cases loose, offensive motions were present, and both had lost weight in spite of good appetite. Liver and spleen were not enlarged. Blood culture was unfortunately not performed. The organism responsible was staphylococcus aureus (coagulase positive).

Group D: Unknown portal of entry. There were four cases in this group. One case had a septic arthritis of the left knee, and 15 ml. of thick pus (staphylococcus aureus) were aspirated. Twenty-four hours after the onset of the swelling of the left knee, septic spots appeared on the skin of the left thigh and paronychiae were present on the right index finger and left thumb. A radiograph of the left knee joint showed no abnormality. Blood culture was not performed because the organism had already been obtained from the left knee joint.

Two cases had osteomyelitis of the maxilla accompanied by severe oedema and cellulitis of the cheek. A radiograph showed no abnormality. Blood culture was not performed because the diagnosis was not in doubt. Clinically these three cases showed no general systemic disturbance, appetite was not impaired, and there was no loss of weight. All three cases responded quickly to treatment with penicillin.

The fourth case in this group was puzzling from the etiological viewpoint, for although the blood culture was positive for B. coli, no source of infection was found. The child was well until the sixth day of life, when she developed a temperature of 104° F. The following day a squint was noticed, but there was no vomiting or twitching. Lumbar puncture showed a sterile fluid. The mother had a temperature of 102° F. after delivery, and this returned to normal with sulphonamides. It is possible that the baby was infected from the mother. This child recovered following penicillin and sulphathiazole therapy.

Discussion

The clinical picture produced by septicaemia of the newborn differs considerably from that seen in older children or in adults. High temperature, rigors, and convulsions are exceptional. As Parsons (1944) has said, ' It is so entirely different from that usually associated with an acute infective illness that it may pass unrecognized by doctors, nurses and paediatricians without special experience.'

Infection in the newborn tends to be generalized, it is often not accompanied by fever, and it may be rapidly fatal within twenty-four hours. Spence (1941) states that the variety of pathogenic organisms is great, but they all tend to produce septicaemia,

with symptoms of drowsiness and disinclination for food, developing sometimes within twenty-four hours of birth, and with localization of the infection as a neonatal pneumonia; or, more typically, an infant may thrive well for a few days, then refuse foods, become drowsy or peevish, and develop a little diarrhoea. Cameron (1929) states that an estimate of the efficiency of the circulatory, respiratory and suction apparatus of the child will serve directly as a measure of the child's general well-being and vitality. Almost all forms of neonatal disorder show themselves as disturbances of one or more of these vital functions: and loss of appetite, with consequent loss of weight in the neonatal period, is probably the most constant sign of neonatal septicaemia. Paterson and Bodian (1946) state that the manifestations of septicaemia may be masked, and clinically may be slight, the infant merely being listless, apyrexial, or failing to take its feeds or thrive.

Since any infection in the newly born, however trivial, must be taken seriously if a high neonatal mortality rate is to be avoided, an evaluation of the clinical features is important.

Diarrhoea occurred in seven of Morison's (1944) nine cases of umbilical sepsis; Leopold (1944) and Brennemann (1945) consider it a constant feature, but in Dunham's (1933) thirty-nine cases no mention is made of it. Diarrhoea was a marked feature in ten cases of the present series, and was present in all six babies suffering from umbilical sepsis.

Loss of weight is an important sign. In Morison's (1944) series all cases showed an abnormal initial fall in weight, with no increase after the fourth day. Leopold (1944) states that the infant loses weight rapidly as a result of loss of appetite, vomiting, and loose stools. Of my fifteen cases, loss of weight occurred in ten, two were not weighed, and in three a gain in weight was recorded.

Jaundice is considered a very prominent finding by Leopold (1944), and Brennemann (1945) states that it is frequently present. It was present in fourteen out of thirty-nine cases recorded by Dunham (1933), including seven of eleven cases of staphylococcal infection and six out of ten cases of B. coli infection. In none of the thirteen cases of streptococcal septicaemia was jaundice present. It occurred in only two cases of the present series; both had umbilical sepsis and the organism was a staphylococcus.

Bleeding occurred in ten of Dunham's (1933) series; in five of the six cases of staphylococcal infection, and in three of the seven infected by B. coli. It occurred in none of the fourteen streptococcal cases. Three of my patients showed a bleeding tendency, all were examples of umbilical sepsis and had a prolonged prothrombin time.

Fever was a feature of thirty-three of the thirty-nine cases recorded by Dunham (1933). In nine cases of the present series temperatures above 99° F. were recorded, and in six cases the temperature rose to over 100° F. Leopold (1944) stated that pyrexia may be absent, slight, or high. Brennemann (1945) considered that the temperature is not characteristic but that fever is usually present at some stage of the illness.

The spleen was felt in only one case of my series. It was palpable in nineteen of Dunham's (1933) thirty-nine cases, and Brennemann (1945) considered that it was nearly always enlarged.

The leucocyte count in nine of the eleven cases of the present series in which this examination was performed showed a range from 10,000 to 20,000 with an average count of 17,000 per c.mm. The other two cases had a leucocytosis of 31,000 and 32,000 per c.mm. A striking feature of all the counts was the high percentage of immature cells. Dunham (1933) recorded figures ranging from 4,000 to 50,000, and the cases with a leucopenia or a leucocytosis above 30,000 carried a poor prognosis. Both my cases with high white cell counts recovered. A differential white cell count to determine the number of immature cells is of more value than the total white cell count, for the absence of leucocytosis does not rule out infection, especially in the neonatal period.

Treatment

Penicillin was given to all the fifteen cases of my series, and seven received sulphonamides in addition. Treatment was started before the nature of the infection or the sensitivity of the organism to the drugs was known.

The dose of penicillin was 3,000 units per pound of expected body weight in twenty-four hours, given in divided doses intramuscularly, but this dose was increased if the organism proved relatively insensitive—for example one case was given 15,000 units per pound per day.

The sulphonamide dosage was approximately 0·25 g. per pound per day.

Bodian (1945) and Couper (1946) have advocated the combined use of penicillin and sulphonamide, and this is of particular value if the organism is B. coli.

The table records the details of therapy.

Florey (1944) originally suggested a standard adult dose of 1,000 units per pound in twenty-four hours, and Bodian (1945) employed the same dose in infants from four days to eleven and a half months old when treating twenty-one cases of bacteriaemia due to staphylococcus aureus (14), β-haemolytic streptococcus (3), staphylococcus aureus, and β-haemolytic streptococcus (1), and staphylococcus albus (2). Fifteen cases (71 per cent.) recovered. Bodian (1946) found that the above dosage gave adequate blood levels of circulating penicillin when divided into four-hourly intramuscular injections in

TABLE

DETAILS OF THERAPY IN FIFTEEN CASES OF NEONATAL SEPTICAEMIA

Number of case	Penicillin		Sulphonamide			Organism	Result
	Units/lb./24 hrs.	Total (Units)	Preparation	G./lb./24 hrs.	Total (g.)		
1	1,000	30,000	Sulphathiazole	0·25	6·5	Staph. aureus	Died
2	3,000	189,000	Sulphamezathine	0·25	6·5	Staph. aureus	Recovered
3	15,000	320,000	Sulphamerazine	0·25	1·25	Staph. aureus	Died
4	6,000	30,000	—	—	—	Haem. strep.	Recovered
5	3,000	50,000	Sulphamezathine	0·5	6·0	Staph. aureus	Died
6	3,000	120,000	Sulphathiazole	0·5	9·5	Staph. albus	Recovered
7	1,000	108,000	Sulphadiazine	0·25	8·0	Staph. aureus	Died
8	3,000	216,000	—	—	—	Staph. albus	Recovered
9	2,000	10,000	—	—	—	Staph. aureus	Died
10	3,000	20,000	—	—	—	Staph. aureus	Died
11	3,000	30,000	—	—	—	Staph. aureus	Died
12	3,000	390,000 and 100,000 into joint	—	—	—	Staph. aureus	Recovered
13	3,000	720,000	—	—	—	Staph. aureus	Recovered
14	3,000	324,000	—	—	—	Staph. aureus	Recovered
15	3,000	243,000	Sulphathiazole	0·25	20·0	B. coli	Recovered

full-term babies and six-hourly in premature infants. Allen (1946) suggested a dose of 1,500 units per pound in twenty-four hours in cases of neonatal sepsis; no penicillin blood levels were undertaken. Couper (1946) suggested a total of 25,000 units in twenty-four hours in divided doses irrespective of weight.

Buchanan (1946) found that 1,000 units per pound in twenty-four hours was an inadequate dose, but that 2,000 units per pound in twenty-four hours was adequate. However, to allow for variable sensitivity and a margin of safety she advocated a dose of 4,000 units per pound in twenty-four hours given by intramuscular injections three-hourly. By employing still higher doses (5,000 units per pound in twenty-four hours) at six-hourly intervals an adequate blood level and satisfactory response to treatment was observed.

It is doubtful whether the blood level of penicillin commonly accepted as desirable must be maintained throughout the entire twenty-four hours, and I suggest that 3,000 units per pound in twenty-four hours given by six-hourly intramuscular injections will be found effective. Sulphonamides should always be given in addition, at least until the nature of the organism and its sensitivity has been determined.

The results of treatment of these fifteen cases are not impressive, only eight cases surviving. In most cases chemotherapy was started within an hour of admission to hospital, and in dosage which, by accepted standards, could be regarded as adequate.

Summary

1. Fifteen cases of neonatal septicaemia seen at a children's hospital in London during 1946 are reported, with clinical findings and pathological investigations.

2. The infrequency of diagnostic clinical findings is stressed. Loss of appetite, failure to gain weight (or weight loss), and diarrhoea are common findings. The temperature is rarely raised above 100° F., jaundice is infrequent, and a palpable spleen is rare. The level of the white blood count is not of value in diagnosis, but the high percentage of immature cells is of considerable importance.

3. Blood culture is an important investigation in a newborn baby who fails to gain weight but in whom abnormal clinical signs are minimal or absent.

4. The treatment suggested is a minimum dosage of 3,000 units of penicillin per pound expected body weight every twenty-four hours, in six-hourly doses intramuscularly; together with 0·25 g. of a sulphonamide per pound per twenty-four hours. This combined treatment should be started before the results of investigations are known.

5. The results of treatment were disappointing. There were eight deaths.

I wish to thank the Honorary Staff of the Queen Elizabeth Hospital for Children, London, for access to the cases, Dr. Eirlys Jefferson and other House Physicians for the detailed case records, and Professor Norman B. Capon for much helpful advice and criticism.

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A STUDY OF NEONATAL INFECTIONS IN THE NURSERIES OF A MATERNITY HOSPITAL

BY

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Infection arising in the neonatal period is recognized as one of the major causes of neonatal mortality. Thus McNeil (1942), in a series of 225 necropsies carried out on infants dying in a maternity hospital, found infection in 27 per cent. Corner (1946) found that in one hospital 25·3 per cent., and in another 29·7 per cent. of all infants became infected. This present study covers a period of fourteen months (January 1, 1946, to February 28, 1947) during which all infections, however trivial, were recorded and investigated with a view to determining their nature and the factors influencing their spread.

The results are shown in table 1. It will be seen that the total number of cross infections occurring was sixty-three while the number of infants at risk was 2,274. The cross infection rate was 2·77 per cent.

Since the prevalence of infection in hospital nurseries is bound to be related to the quality and the sufficiency of staff available for their care, and the nature of the accommodation provided (and it is the writer's belief that this represents the relative importance of factors) a summary of nursery conditions is given.

Staff

Medical. In addition to the visiting and resident obstetric staff, the paediatric staff consists of a paediatrician who sees all infants daily, and a resident medical officer. In addition to the care of the nurseries, the latter attends all Caesarean sections and difficult forceps deliveries and is called if difficulty is anticipated in resuscitating any infant.

Nursing. The staff consists of a superintendent midwife, twelve sisters, nine staff nurses, and forty-five pupil midwives, all of them state-registered nurses. Taking into consideration those in the labour ward, those on district, and the extra staff needed in the premature unit and sick nursery, this leaves a sister and staff nurse for each lying-in flat, and two day and one night nurse for a six-bed unit and two side wards. Allowing for off-duty, this means that for a considerable part of the day one nurse may be responsible for up to nine mothers and babies. It is considered essential that mother and child should be regarded as a single unit, and the same staff therefore care for both.

Domestic. Each flat has two orderlies who help with meals, sweep and dust, but perform no nursing duties. There is also a cleaner on each flat for scrubbing and rough work.

Special 'anti-infection' training. Pupil midwives usually arrive in small batches and are interviewed individually on arrival. The special problems involved in the nursing of the newborn, the risk of infection, and the measures adopted to minimize it are discussed. Special emphasis is laid on the nurse's duty to report any deviation from her normal health, and especially any respiratory or skin infection or any gastro-intestinal symptoms. At least twice a year a demonstration is given on the lines suggested in the Medical Research Council War Memorandum No. 11 (1944), the following cultures being shown: (a) from hands before and after washing; (b) from hands after using a handkerchief (showing the degree of contamination and the consequent necessity for washing); (c) from the pocket in which a handkerchief is carried (to show the risk of carrying anything else—pen, scissors, etc.—in the same pocket; (d) from a gown worn while changing a baby (to show how organisms would be transferred from one baby to another if a separate gown were not worn for each); (e) from plates exposed during sweeping, bedmaking, etc. (to show the number of organisms which must be deposited at these times on all exposed surfaces, and indicating the need for putting all equipment away when not actually in use).

There is no doubt that visual demonstrations of this kind help the nursing staff to realize that the rigid barrier-nursing technique enforced is of real value and not just an irritating ritual.

Accommodation

The maternity service of the hospital accommodates fifty-nine mothers and babies on the first and second floors of a modern block (1934) and in the original maternity block (1892). When admissions rise above this level, overcrowding can only be avoided by transferring cases to a block which used to form part of the workhouse infirmary. Except in this annex, the basic unit is one of five

or six beds, allowing 120 square feet for each mother and child. On the first floor the cots are beside the mothers' beds. On the second floor they are partly screened off at the end of the ward by a seven-foot glass and wood partition with a central doorway but no door. In the old block, there are two lying-in wards of five beds each, and a separate nursery containing ten cots but divided internally into two units of five cots. There are also in the hospital eleven small wards, seven double, and four single. The annex is a vast undivided ward 144 feet by 48, and the 'nursery' is demarcated only by ordinary ward screens. The 'premature' unit consists of a nursery, and a mothers' ward and bathroom. Wood and glass partitions form 'stalls' 7 by 4 by 4 feet for ten babies. On occasion the more mature infants are placed in the mothers' ward. The sick nursery can hold six infants but is rarely filled.

Every nursery and practically every side ward has a handbasin with elbow taps, and there are also five handbasins in the corridors. The annex is less well provided. The handbasins are at each end of the ward and have not elbow taps. Contamination is avoided by using toilet paper to turn on the taps so that they are not touched by soiled hands.

Routine Care in Normal Nurseries

This is based on the assumption that every baby is a potential danger to every other baby. It is believed that to apply a barrier-nursing technique only to infected babies is to be wise too late.

Each infant's toilet requirements are kept separate. Peanut oil for the initial cleansing, lanoline, and cord powder, are sterilized in small individual containers. Bathing is not practised but the buttocks are cleansed at each changing time using sterile water, sterile swabs (each used once only and discarded), and individual bowls, boiled after use. Cot blankets and baby clothes have been, since October 1, 1946, autoclaved after their return from the laundry. Linen and clothing from the sick nursery is autoclaved before being laundered.

A gown is kept at the foot of each cot and is worn by the nurse when handling the baby for any purpose. Thus, before a baby's feed, the nurse washes her hands, puts on the gown provided, picks up the baby, changes him (on her knee), carries him out to his mother, takes off the gown, and returns it to the cot, before washing her hands again and starting on the next baby. Hands are washed and gowns donned again to bring the babies back after feeds. 'Scrubbing up' is not required, as plates inoculated with swabs taken from hands thoroughly washed and dried on clean towels show very few organisms. Repeated scrubbing, moreover, makes it much more difficult to keep the hands in good condition. A 'barrier cream' (Innoxa BQ7) is issued to each nurse at regular intervals and has been very effective in preventing chapped hands.

Masks are not worn as a routine, because stocks are inadequate to allow of their being changed sufficiently often to be a real protection. Reliance is placed on avoidance of loud talk, laughing, coughing, etc. Nurses report the least suspicion of a respiratory infection, and can be employed apart from babies or sent off duty. Masks are worn constantly in the premature unit, and in nursing infectious cases (for example septic spots) to try and prevent the development of a carrier state.

The medical round begins in the premature unit, where a clean gown is put on; the healthy nurseries are then visited, and then any nursery suspected of being infected (having recently had a case of infection in it), the gown being discarded here. If all nurseries are clean of infection, the same gown is worn throughout and discarded in the sick nursery. For emergency visits the ward concerned provides a fresh gown. Doctors and students follow the same hand-washing rules as the nurses, but do not change their gowns unless an infant has actually been in contact with the gown. Short sleeves are worn. A special (coloured) gown for the cleaner is kept in each ward and not worn elsewhere.

Floors are oiled as recommended by Thomas (1941), and damp dusting is used. All equipment is put away or covered when not actually in use. A length of gauze covers the gap between the top of the bedclothes and the end of the cot.

The number of deliveries is such that a six-bed unit can usually be filled within twenty-four hours, and therefore all mothers and babies in any one ward are ready for discharge at practically the same time (Caesarean sections, etc. are mainly nursed in side wards). As each ward empties, the linen is sent for laundry, blankets and mattresses for steaming, beds, cots, and mackintoshes are carbolized, and the floor is scrubbed and oiled. The beds are then made up and the ward aired for twenty-four hours.

Feeding

The greatest efforts are made to ensure full breast feeding, and a healthy spirit of emulation between the nurseries is maintained by a chart to which all the staff have access. On graph paper a square is filled in daily for each baby: blue for a day on which it has been wholly breast fed; yellow if any complement has been given. During the first forty-eight hours of life, sterile water is given in addition to the breast feed. Since December 1, 1946, this has been given by spoon.

After each feed, mothers express any surplus milk, which is sterilized and used in the premature and sick nurseries as required.

As the hospital receives a high proportion of emergencies and abnormal cases, it is not always possible to secure full breast feeding, and artificial feeds (complementary or complete) of dried milk are used. Since October 1, 1946, these have been prepared in the milk kitchen.

Milk Kitchen

No one may enter here except those on duty (a permanent sister, and a pupil midwife), the superintendent midwife or her deputy, the paediatrician, and the resident medical officer in charge of infants.

After feeds, bottles are placed by ward nurses on a ledge outside a hatch marked ' bottles in.' They are taken in, washed in the first sink, rinsed in the second, and packed into a bottle sterilizer. After sterilization they are transferred to the ' clean ' side and the feeds are prepared, the staff wearing gowns and masks. The bottles are covered with cellophane secured by rubber bands, labelled, and placed in the ' feeds sterilizers.'

At feeding time each ward is issued with a tray containing its feeds, teats in a sterile bowl (the nurses prefer to have an assortment of teats from which to choose for each baby, rather than to have the teat put on the bottle by the milk kitchen staff), spoons in a sterile jar, the whole covered with a sterile towel and issued through a hatch marked ' feeds out.'

TABLE 1

TABLE GIVING STATISTICS OF CROSS-INFECTION OCCURRING IN A MATERNITY HOSPITAL OVER A PERIOD OF FOURTEEN MONTHS

No. of cases in hospital Jan, 1, 1946, to Feb. 28, 1947	2,274
Range of duration of hospital stay	1–65 days
Average duration of hospital stay	10·3 days
Average duration of hospital stay before infection	7·4 days
Average estimated increased length of stay as result of infection	1·8 days
Total no. of cases with cross-infection	63
Percentage of cases with cross-infection	2·77
Types of cross-infection:	
gastro-enteritis	Nil
upper respiratory infections	1
lower respiratory infections	1
other infections	61
No. of deaths attributable in whole or in part to cross-infection	2

Assessment of Infection

As will be seen from tables 1 and 2, most infections were manifest on inspection. Of these, it is only necessary to mention that so far as skin lesions were concerned the smallest single pustule was recorded as an infection. Any eye which appeared at all moist was swabbed and recorded as an infection if pus cells were present, whether or not organisms were isolated.

The mouth was inspected by the nurse before each feed, and daily by one of the paediatric staff. Apart from these obvious infections, any infant whose progress was in any way unsatisfactory, with special reference to vigorous feeding, normal bowel action, steady weight gain, and contentment, was examined critically and bacteriological investigations carried out when indicated. The routine measures taken included nasal, throat, and rectal swabs, and examination of a clean (non-catheter) specimen of urine.

In two cases the presence of infection, evident clinically, was confirmed at autopsy. Permission for post-mortem examination was sought in all cases of neonatal death and obtained in forty-one instances (70 per cent.). Apart from three cases of definite intra-partum pneumonia not included in this series, no evidence of infection was found.

In addition to the ordinary records, each case of infection was marked as a red square on the feeding chart already mentioned. This was expected to emphasize any tendency to a series of cases arising in any one nursery, but, in fact, no such series occurred. The chart did, however, furnish graphic evidence of the relative incidence of cross-infection in nurseries of different types.

It will be seen from table 2 that fifty-three (84·1 per cent.) of all infections were due to staphylococcus aureus. Of these, skin lesions numbered thirty-six (57·1 per cent.). This predominance of

TABLE 2

ANALYSIS OF INFECTING ORGANISMS

Infection		Number of cases
Staphylococcus aureus		53
Skin lesions		36
Single septic spots	15	
bullous impetigo	16	
furuncles	4	
paronychia	1	
Conjunctivitis		9
Styes		4
Dacryocystitis		1
Rhinitis		1
Umbilical sepsis		1
Septicaemia		1
Monilia albicans		8
Doubtful		2
Coryza		1
Pneumonia		1

staphylococcus aureus infections is, of course, well known and has been described by many workers. Thus, Elliott et al. (1941) recorded an outbreak of pemphigus neonatorum which involved twenty-two infants, two mothers, and one nurse; Benians (1943) had 162 cases of bullous impetigo during a period of four months; while Corner (1946) reported a skin infection rate of 25·3 per cent. The vast majority of cases cause no constitutional disturbance, but this is no guarantee that serious or even fatal illness may not develop. In this series no deaths occurred, but one case of serious illness (Baby G., vide infra) was recorded.

The only other organism responsible for multiple infections was Monilia albicans, present in eight cases (12·7 per cent.). The total incidence among all infants was 0·35 per cent. This is not a high

incidence; Ludlam and Henderson (1942) found it in 6·4 per cent. of their cases, but the loss of one infant out of eight impels us to take it very seriously.

The single case of pneumonia occurred in a premature infant, birth weight 2 lb. 7 oz., admitted from outside the hospital service. This infant was tube-fed and was on continuous oxygen until its death on the sixteenth day was heralded by cyanosis, rapid respirations, and a rise in temperature. No physical signs were detected in the lungs, but autopsy showed consolidation in the right lower lobe.

Table 1 shows that the average increased duration of hospital stay as the result of cross-infection was only 1·8 days. This is not in itself important, if cross-infection were wholly eliminated it would release accommodation for only nine more cases each year. There were, however, one case of serious illness and two deaths attributable in whole or in part to cross-infection. These ought not to have occurred.

Sources of Infection

Every person who had come into contact with an infected infant, including, of course, the labour ward staff, was examined and had nasal and throat swabs taken for culture. It was not possible to have serological typing of staphylococci carried out, and it was assumed, therefore, that any staphylococcus aureus giving a positive coagulase reaction was significant.

In ten cases pathogenic staphylococci were recovered from the mother, who in nine cases had skin lesions on face or arms which antedated the baby's lesions. In the tenth case, Mrs. G., an elderly primipara, developed puerperal pyrexia, staphylococci being isolated from a cervical swab. Baby G. on his fourth day of life developed a purulent bulla on his right index finger and had a moist unhealthy cord, staphylococcus aureus being cultured from both sites. Subsequently the baby became extremely ill and dehydrated, with fever, vomiting, abdominal distension, and rapid respirations. Intravenous fluids, sulphonamides, and penicillin (then in very short supply) were followed by recovery but the baby had the narrowest possible escape.

In none of these ten cases was staphylococcus aureus isolated from any member of the staff who had been in contact with mother or child.

In thirteen cases nurses appeared to be possible sources of infection. One had a pustule on her cheek, covered by an occlusive dressing. She was nursing the infant whose infection is recorded as umbilical sepsis. Failure to feed on one occasion, and one loose motion, were associated with staphylococcus aureus in the swab from the umbilical stump. The baby's illness was trivial. In the other instances staphylococcus aureus was isolated from the nasal swab of a symptomless carrier.

Five babies must be presumed to have acquired their infection before birth, for a pustular rash from which pathogenic staphylococci were isolated was present at delivery, the swabs being taken in the labour ward. These cases might, perhaps, have been excluded from the series.

These twenty-eight staphylococcal infections were all in which it was felt that the source had been traced with any certainty.

Trauma was believed to be responsible for four cases of thrush which occurred almost simultaneously in two nurseries. A batch of teats was issued which were made of very harsh red rubber. Every baby wholly or partly bottle fed with these teats developed an abrasion on the hard palate.

Baby S. was delivered normally. He was given one feed of sterile water because it was thought that his mother was still too exhausted to see him. Staphylococcal infection was superimposed on his thrush lesion; within twenty-four hours signs of pneumonia were present, and in forty-eight hours he was dead. Autopsy confirmed the presence of pneumonia, but it was suggested that the appearances were suggestive of an intrapartum infection since the lungs contained much aspirated vernix. Since, however, the possibility of post-natal infection cannot be excluded, the case is included in this series.

TABLE 3

PROBABLE SOURCES OF INFECTION

Probable source of infection	No. of cases	Per cent.
Mother	10	15·8
Nurse	13	20·6
Trauma	4	6·3
Intrapartum	5	7·9
Untraced	31	49·4

It is of course arguable that, since swabs were only taken from nurses who had been in contact with infected infants, the carrier-state had been contracted from the child: or, alternatively that, in view of high carrier-rates commonly reported, these findings were only coincidental. Thus Gillespie and others (1939) found staphylococcus aureus in nasal swabs from 43·4 per cent. of hospital students, and McFarlan (1938) found the rate for adults in hospital to be 42 per cent. This is supported by the fact that in February, 1946, nasal swabs of all hospital personnel showed that 19·3 per cent. were carriers of pathogenic staphylococci. In other words, the carrier rate among nurses associated with cases of cross-infection was not significantly higher than that among the hospital staff in general. Moreover, if a nurse were the source of infection one would expect more than one case to arise among her patients. Thus, in the epidemic already referred to, Elliott and others (1941) considered that their twenty-two babies and two mothers had probably been infected by a single nurse. In this present series there was no epidemic spread, the maximum incidence in any one nursery

FIG. 1.—Numbers of infections each month expressed as percentage of total admissions.

being two cases, and this multiple incidence occurring only three times. This also tells against any serious case-to-case spread of infection. It must be admitted, however, that there was not much opportunity for this type of spread since, as has been said, each unit was emptied, cleaned, and aired after each batch of babies.

A possible seasonal incidence was next considered. It was thought that this might arise in two ways. There is a higher incidence of catarrhal infections during the cold, wet months and this would certainly increase the dispersion of organisms by droplet spread. There is less enthusiasm for widely open windows in the winter. Fig. 1 seems to support this, or at least to show a peak in February and a minimum incidence in July, with relatively few cases in March and May. This figure, showing the actual number of cases, is open to the criticism that if there were many more admissions in one month than another one might reasonably expect more cases of infection. If the results, however, are shown as a percentage of the cases at risk (fig. 2) a similar distribution is seen.

In connexion with this question of increased admissions, it might be expected that, since staff remains practically constant, any large increase in admissions might lead to a rise in the cross-infection rate by imposing extra work and therefore limiting the time available for each patient. Fig. 3, where the number of admissions each month are shown together with the infection rate expressed as a percentage of total cases at risk, does not suggest that there is any significant relationship between the figures. Or, in other words, it would seem that a larger influx of work than has yet been experienced (minimum admissions in one month, 127, maximum 218) is needed to saturate the defences.

FIG. 2.—Actual numbers of infections occurring each month.

Another way in which the increased number of admissions might be expected to operate adversely would be by reason of overcrowding. In the main hospital this is impossible, as it is a rule that no extra beds are ever placed in wards. The overload is distributed by transfers to the annex, which can receive up to twenty mothers and babies. Four cases of infection occurred during the year. The numbers of babies at risk when these cases occurred were 5, 8, 11, and 11, so that overcrowding does not seem to have been a factor.

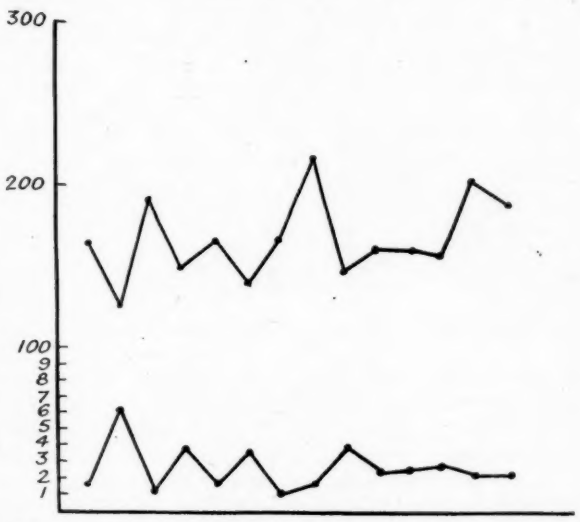

FIG. 3.—Upper line: number of admissions each month. Lower line, per cent. of infants developing infection.

It is unlikely that changes in staff played any part in the production of cross-infection. New pupils come in twos and threes and there is sufficient permanent staff to enable them to be supervised carefully until nursery routine becomes second nature.

Nursery Design

When we consider the various types of nursery to which normal infants are admitted, it appears that there is a very significant difference in their cross-infection rates.

It appears that the rate is highest where babies are kept beside their mothers, whether in six-bed units or small side wards. The side wards show only slightly better results, but it must be emphasized that the majority of mothers nursed in these wards present some medical or obstetric abnormality and that their babies are therefore exposed to a somewhat

greater risk. It must be admitted, however, that the rate of staphylococcal infection among these mothers appeared to be quite insignificant.

Segregating the babies behind an incomplete partition lowers the infection rate still further, but the steepest fall occurs where the nurseries are entirely separate from the lying-in wards. The only essential difference in this unit is that the hazard of dust-borne infection, due to bed-making and sweeping, is eliminated. In all other respects the nursery routine is identical with that in other parts of the hospital. It is the firm conviction of the writer that this separation is psychologically undesirable, but it certainly gives the best results as regards cross-infection. In discussing the epidemiology of an outbreak of pemphigus neonatorum Allison and Hobbs (1947) draw attention to the probable advantages of reducing the number of infants at risk in any one nursery, and suggest

TABLE 4
INFECTION RATES IN VARIOUS TYPES OF NURSERY

Type of nursery	Total no. of babies at risk	Cases of infection	Per cent. of cases becoming infected
Cots beside mothers' beds	456	21	4·6
Cots partly screened off ..	647	19	2·76
Side wards ..	298	10	3·69
Separate nurseries	462	5	1·08
Annexe (open ward) ..	293	4	1·02

single rooms or cubicles for mother and baby. They feel that the chief risk is from nursery infection transmitted mainly by the nurse. It is suggested by this present study that these risks can be largely reduced by strict care but that fluff and dust from the mothers' beds form an important vehicle for infection. It should be possible to design a unit which would enable babies to be within their mothers' view, and yet completely separated from the fluff and dust of the ward. Whether this arrangement would be emotionally satisfying to the mothers, or whether the relatively small risk of cross-infection should be accepted, is outside the scope of the present inquiry.

It is interesting to note that the cross-infection rate in the annex approximates very closely to that in the small separate nurseries. At first it was thought that this might be due to the fact that patients are not transferred until at least the fourth day after confinement. There was an impression that most infections had become manifest before this time and that consequently the period of greatest risk was past before transfer took place. It was found, however (fig. 4) that the bulk of infections developed between the fourth and eighth day, with a peak on the sixth day, so that this explanation is inadequate. The important point seems to be the vast size of the ward and its excellent ventilation, as though empty space were as good a barrier against infection as bricks and mortar. This is, of course, the basis of barrier nursing as originally described by Rundle and Burton (1912). In the opinion of the writer, however, it would be wrong to draw the conclusion that units containing so many mothers and babies, either together or separately, are satisfactory, if only because, in the event of serious infection occurring, it is impossible to close down so many beds without disrupting the

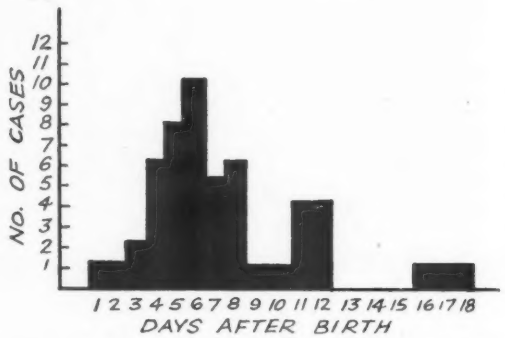

FIG. 4.—Ages of infants (in days) when infection developed.

work of the hospital, a disadvantage which of course attaches equally to the large general nursery so common in maternity hospitals. During the period of this investigation no case, for instance, of gastro-enteritis occurred, but its incidence in such a unit might have been disastrous and the risk should not be taken from choice.

Summary

A description is given of the precautions taken against cross-infection in a maternity hospital where four different types of nursery are in use.

The general cross-infection rate over a period of fourteen months was 2·77 per cent.

It is shown that the staphylococcus aureus was responsible for fifty-three out of sixty-three infections occurring among 2,274 infants.

The various factors contributing to the prevalence of cross-infection are examined. It appears that, other factors remaining constant, nursery design exerts an important influence. The small, separate, nursery would seem (from the point of view of preventing infection) to be the most satisfactory.

In the last resort, results depend on the maintenance of an efficient barrier-nursing technique. This should operate in all nurseries. To apply it only to cases already infected is to be wise too late.

My thanks are due to Dr. J. T. Lewis, bacteriologist to the hospital, for reports on innumerable swabs; to Dr. J. G. Morison for pathological data;

to Drs. Craven, Stevenson, and Sullivan for painstaking observation and record-keeping; and above all to Miss McKee, Superintendent Midwife, and all her staff for unending enthusiasm and perseverance.

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THE OCCURRENCE OF OEDEMA IN INFANTILE GASTRO-ENTERITIS

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The occurrence of oedema during infantile gastro-enteritis has been noted in the past by various writers, but few have provided detailed descriptions of the condition. Arabian writers (seventh century A.D.) record that ' in the course of the disease, the child may become bloated throughout the body or in part '; and Rush, in the eighteenth century in America, observed that ' during summer diarrhoea a swelling frequently occurs in the abdomen and limbs.' Hume (1911) appears to be the only writer who has described symptomatology and discussed etiology in some detail. In a paper entitled ' General Oedema following Gastro-enteritis in Children,' he described thirteen instances of the complications in children of ages ranging from one to four years, who developed oedema of the hands and feet three to four weeks after the onset of an attack of diarrhoea and vomiting. More recent references provide little additional information. Graham and Morris (1933), Kutumbiah (1941), and Dieckhoff and Künstler (1944), make only brief comment on the occurrence of the phenomenon, as do Thomson and Findlay in their textbook on children's diseases. In other modern paediatric textbooks, however, although descriptions are given of ' overhydration oedema ' following excessive parenteral fluid administration and of ' nutritional oedema ' in marasmus and the wasting diseases, the oedema of gastro-enteritis per se is not even mentioned.

Present Investigation

In view of the scarcity of information on the subject further study seemed desirable. This was begun in the infantile gastro-enteritis wards at Belvidere Hospital, Glasgow, in the summer of 1945.

The following plan of investigation was adopted:

1. All routine admissions to the wards were observed closely for the occurrence of oedema. The nursing staff, especially the morning staff who bathed the babies, were advised to be on the alert for its presence.

2. When it was noted, the patient was weighed immediately and, thereafter, daily records were started.

3. Careful notes were taken of the course of the oedema and of the concomitant clinical features.

4. Feeds of a protein hydrolysate, = ' casydrol,' were given to alternate patients (a) on admission and (b) at the onset of oedema. The purpose of this feeding experiment was to discover whether protein feeding was of value as a means of prevention or of treatment of the condition; this would be a test of the validity of the hypothesis that the oedema was due to hypoproteinaemia of nutritional origin.

General Description of Cases

A total of 176 patients were observed in the infantile gastro-enteritis wards between June 11, 1945, and Jan. 1, 1946. They presented the usual age-incidence found in the disease, 87 per cent. being under eighteen months old. Sex-incidence was the normal 3 : 2 male preponderance. Clinical features accorded with those customarily found in gastro-enteritis, inasmuch as vomiting, frequent stools, and dehydration of varying degree were present. Parenteral infections, mainly respiratory, were noted in 46 per cent. of cases. Although the severity and stage of illness varied from case to case, all exhibited evidence of toxaemia or dehydration or both, sufficiently grave to warrant admission to hospital.

Treatment followed the usual lines. After an initial starvation period, when only saline or 5 per cent. glucose in $\frac{N}{2}$ saline feeds were administered, every alternate patient was given ' casydrol ' feeds. Milk feeds, diluted as required in half-normal saline, was the alternative diet, and this was given also to those infants who could not tolerate ' casydrol.' The feeds were then built up gradually until a full dietary suitable for the patient's age could be administered. All patients received vitamin B complex tablets and vitamin C (50 mg.) tablets three times a day and daily inunction of adexolin ointment (20 per cent.). Sulphadiazine and sulphaguanidine, and, in a few cases, penicillin, were administered where indicated. When necessary gastric lavage was performed, and fluid replaced by

'intragastric' drip (Berkeley, 1947) or by parenteral routes.

Description of Oedema Cases

Clinical features. Among these 176 cases, no fewer than thirty-five exhibited oedema in one or more situations during their stay in hospital. The first indication of the oedema was usually on the dorsal surfaces of the feet and hands. The swelling was of rapid onset and development. It did not readily pit on pressure, but rather imparted a feeling of resilience to the examining fingers. This oedema of the feet and hands was a feature of all the cases, although not infrequently the loose tissues round the eyes were involved, and, more rarely, oedema was noted in the sacral region. In several patients the abdomen seemed distended, and some free fluid may have been present. The urine of all oedematous patients was clear; and in no case was abnormality found in the cardiovascular system. Indeed, apart from the weight changes (which are described below) no other outstanding clinical abnormalities could be detected in the oedematous patients. Most of these infants, however, showed some degree of microcytic hypochromic anaemia (Hb ranging from 40 to 70 per cent., red blood cells from 3 to 4·5 million and white blood cells from 6,000 to 13,000 cells per c.mm., and films showing normal cells or ring-staining microcytes). Although parenteral administration of fluid was pursued in all acutely dehydrated patients, this form of treatment was required soon after admission, and in no case did oedema develop during the administration, or within the seventy-two-hour period following. Thus the oedema which was being observed was not the well-recognized type of 'overhydration oedema' which is due to administration of excess parenteral fluid.

Three cases had received intragastric drip therapy before the onset of oedema. The fluid administered was 5 per cent. glucose in $\frac{N}{2}$ saline and daily volumes of 30 ml. per kilo of body weight had been introduced.

The general treatment of the oedematous patients differed in no way from that of the non-oedematous, but approximately half the oedematous patients were fed on 'casydrol,' the remainder continuing to receive their previous diet, which in most cases was diluted milk feeds.

Course of oedema. The course of the oedema was unexpected. Spontaneous subsidence of the oedema occurred in all cases except in four infants who died while oedema was still present. This occurred even in patients whose dietary and therapeutic regime had not been altered. The duration of visible oedema in most cases was found to range from two to eight days. Recurrence of oedema was noted in only one case. Here the initial oedema had lasted for two days; seven days later it recurred on hands and feet, and again subsided after four days. This child subsequently was discharged well.

Prognosis. Of thirty-five oedematous patients, eleven died (31·4 per cent.), whereas of the 141 non-oedematous patients, twenty-five died (17·7 per cent.). Although a χ^2 test showed that there was no significant difference between these death rates, the clinical impression was that oedematous patients had a poorer prognosis than the non-oedematous.

In four fatal cases, oedema was still present when death occurred. The remaining seven fatal cases were oedema-free at the time of death, the time interval in these cases, between the subsidence of oedema and the onset of death, being from seven to fourteen days.

Post-mortem examinations. Two of the fatal cases were examined post mortem. In one child no obvious lesions were found; in the other, who died while oedema was still present, histological examination of liver by Dr. Reynolds (Pathologist to the Glasgow Corporation Public Health Department) revealed extensive fatty degeneration.

Weight changes. Weight changes were a striking feature found in almost all the cases, and they provided objective confirmation of the presence and course of the visible oedema. A high increase in weight appeared with the onset of the oedema. The maximum increase occurred within twenty-four hours of onset; subsequently, the weight chart showed a downward trend corresponding with the diminution of the visible oedema. The weight increases accompanying the oedema varied from 4 to 58 oz., the average being 22·1 oz. with standard deviation $\pm 11 \cdot 9$. The initial losses in weight which occurred simultaneously with the subsidence of the visible oedema were rapid and were accompanied by diuresis. The figures varied from 7 to 30 oz., the average being 16·8 oz., and standard deviation $\pm 7 \cdot 8$. Subsequently, during the following seven to fourteen days, most patients continued to lose weight, although in amounts not as high as the initial weight loss.

Detailed Analysis of Oedema Cases

Oedema-incidence and age of patient. Table 1 shows that oedema was confined to patients in the 0 to 16 months' age group, and that 83 per cent. of the oedema cases were one year of age and under.

Oedema-incidence and duration of illness. Oedema was never observed during the first four days of the patient's illness. Thereafter it occurred in six cases (17·1 per cent.) during the fifth to seventh days of illness, that is, during the first week; in nineteen cases (55·7 per cent.) during the second week of illness; in five cases (14·3 per cent.) during and after the fourth week of illness.

Duration of visible oedema. The oedema subsided spontaneously. Four patients died while oedema was still present. In the remaining thirty-one oedematous patients, the duration of visible oedema in twenty-nine patients was from two to

TABLE 1
OEDEMA-INCIDENCE AND AGE OF PATIENT

Age in months	Total cases	Oedema cases	Percentage of oedema cases
0-3 ..	46	8	17·4
4-6 ..	33	8	24·2
7-9 ..	26	9	34·6
10-12 ..	16	4	25·0
13-15 ..	19	5	26·3
16-18 ..	13	1	7·7
19-21 ..	14	0	0
22-24 ..	1	0	0
25-27 ..	8	0	0
Total ..	176	35	19·9

eight days, and in twenty-three patients the duration was only from two to five days.

Oedema-incidence and type of feed given on admission. It had been intended to give 'casydrol' feeds to alternate patients on admission, but some patients could not tolerate 'casydrol' and these were given diluted milk feeds instead. Thus, only one in three of the total patients received protein feedings on admission. Table 2 shows that, despite 'casydrol' feeding, ten infants developed oedema. Also, the incidence of oedema in casydrol-fed patients was little different from the incidence in milk-fed infants. It can be concluded that 'casydrol' feeding was ineffective in preventing oedema.

Casydrol and treatment. After the onset of oedema, alternate patients had been given 'casydrol' feeds, so analysis of the oedematous patients' dietary showed the following four groups of patient:

GROUP 1 consisted of eighteen patients who had been given milk feeds before onset and milk feeds after onset of oedema.

GROUP 2 consisted of eight patients given milk before and 'casydrol' after onset of oedema.

GROUP 3 consisted of six patients given 'casydrol' before and 'casydrol' after onset of oedema.

GROUP 4 consisted of one patient given 'casydrol' before and milk after onset of oedema.

The average duration of oedema was: group 1, 5·11 days; group 2, 4·82 days; group 3, 4·67 days. The duration of oedema in the patient in group 4 was 4 days. Groups 1, 2, and 3 showed no significant difference between their mean duration of oedema.

TABLE 2
OEDEMA-INCIDENCE AND TYPE OF FEED GIVEN ON ADMISSION*

Type of feed given on admission	Total no. of cases	Cases who developed oedema	
		No.	%
Diluted milk ..	113	23	20·4
'Casydrol' ..	61	10	16·3

* Two patients who developed oedema within forty-eight hours after admission are not included in this table.

Duration of oedema and sulphonamide treatment. Of the thirty-one oedematous patients, eight had received no drug treatment (group A), twelve had received sulphaguanidine (group B), and eleven had received sulphadiazine (group C). The mean duration of oedema in group A was 5·0 days, in group B 4·2 days, and in group C 4·8 days. Statistical analysis showed no significant difference between these means. Thus, sulphonamide therapy did not influence the duration of oedema.

Four patients who died while oedema was still present, are not included in this analysis.

Discussion

The paucity of literature on an apparently not uncommon condition is puzzling, but it should be noted that this complication of infantile gastro-enteritis is typically unobtrusive. The oedema appears rapidly and subsides spontaneously and swiftly: it occurs usually after the acute stage has subsided and is not accompanied by obvious change in the clinical picture. It seems possible that observers not specially on the look-out for the condition may have missed its occurrence or regarded it as being less frequent than it actually is.

Weight changes. The weight changes, which were positive confirmation of the visible oedema, varied greatly among the individual patients. The range of weight increases found here accord with the range of spurious weight gains found in nephritis, serum disease, and oedema of premature infants (Holt) and in overhydration oedema following excessive parenteral fluid therapy (Brown et al, 1943).

Etiology. The etiology is obscure and has not been solved by the present investigation. However, some findings of negative value have emerged, and it may be worth while reviewing these and then discussing the possible causes which remain.

Nutritional hypoproteinaemia. Although this hypothesis is favoured by Graham and Morris (1933), the findings in the 'casydrol' experiments do not support this view. The 'casydrol' feeding provided an adequate protein intake, but did not prevent the occurrence of oedema and was ineffective in shortening the oedema's duration. While it might be argued that the 'casydrol' was not absorbed by the severely ill patients on account of rapid peristalsis or derangement in gastro-intestinal function, this argument is refuted by the experiments by Shohl (1943) who found that despite the presence of vomiting, diarrhoea, and acidosis, nitrogen was absorbed and retained when given orally in the form

of casein hydrolysate. Also, in the present series, oedema usually occurred when normal gastro-intestinal function and presumably normal absorption were present.

Therefore, it seems unlikely that nutritional hypoproteinaemia is a major factor in etiology.

Vitamin B deficiency. Likewise, vitamin B deficiency does not appear to be a major etiological factor. There is no proof that the vitamin B preparation which had been administered as a routine to all patients during their stay in hospital had been absorbed. On the other hand, had vitamin B deficiency occurred to an extent sufficient to cause oedema, other signs of the deficiency would have been present, and these (described by Fehily, 1947) were never observed in the oedematous infants.

Possible causes. Albuminuria, heart disease, and macrocytic anaemia (described by Holmes, 1945), are other possible causes of oedema, but were never found in the patients in the present series.

'Overhydration oedema' due to administration of excessive amounts of parenteral fluid has already been excluded as a cause of the condition.

Hume (1911) suggested that the oedema was related to a deficiency in secretion of the suprarenal glands, for he found fibrosis in these glands in two cases at necropsy. He also reported that oedematous children, treated by injections of adrenaline hydrochloride, appeared to show improvement. However, in view of the characteristic tendency of the oedema to spontaneous cure—as observed in the present series—the therapeutic efficacy ascribed to adrenaline injections is open to doubt.

The remaining possibilities. When the above have been excluded from the list of possible causes, the range of hypotheses is narrowed, and attention can be focused on the possibilities which remain. These are: (a) impairment in function of capillary endothelium, (b) impairment in liver function, and (c) impairment in renal function.

Impairment in Function of Capillary Endothelium

Damage to the capillary endothelium is well recognized as a cause of oedema. Dieckhoff and Künstler (1943) favour this hypothesis to account for the oedema of gastro-enteritis, and Sheldon (1943) stated that 'oedema which occurs in marasmic and severely-wasted infants is attributable to changes in permeability of the capillaries resulting from their poor nutrition.' The oedema of acute nephritis appears also to be due to this cause, since the oedema-exudate has a high protein content (usually over 1 per cent.) and changes in the peripheral vessels can often be found (Cumulative Supplement, British Encyclopaedia of Medical Practice, 1947).

Unfortunately there is no scientific evidence to confirm that capillary damage is a cause of oedema in infantile gastro-enteritis. Also some features of the condition are not readily explained by the hypothesis. Thus, if the oedema were due only to the effect of toxaemia on the capillaries, it should surely have become manifest at the early stage of the illness when toxaemic effects were maximum, rather than during the second and third weeks when the oedema usually occurred. Also, if the spontaneous subsidence of oedema is to be accounted for by the rapid recovery of capillary function, the reason for this rapid recovery is not quite clear.

It must be concluded that although impairment of capillary function is a possible cause of oedema, it does not alone account for all the observed features of the condition.

Impairment in liver function. Impairment in liver function is another possible cause of the oedema. In infantile gastro-enteritis, liver damage is a common—in fact, the only common—finding at autopsy; and Thompson (1936) and Lawrence (1946) have brought evidence to show that the occurrence of liver damage may impair the manufacture of serum protein and result in hypoproteinaemia and oedema. On this basis, the spontaneous subsidence of the oedema would be due to the occurrence of compensatory regenerative changes in the liver.

However, there is at present no available data on the fluctuations of the serum protein levels in infants before, during, and after the occurrence of oedema. Until this information is obtained, the hypothesis of liver damage remains a possible but purely theoretical cause.

Impairment in renal function. The important experiments by McCance and Young (1941) on the kidney function of infants have demonstrated clearly the relative inefficiency of these organs during the first year of life. These workers showed that, at low urine flows, the concentration of solids in the infants' urine does not increase as it would do in adults, and that, if oliguria occurs as a result of dehydration, some degree of salt and water retention inevitably occurs. Simmons (1944) has summarized the situation in these words: '. . . the infants' urine is always a dilute urine. Therefore, any infant short of water is likely to have renal failure with retention of salt and urea, and with oedema due to salt-bound water.' It is thus apparent that infants with gastro-enteritis who suffer from oliguria are liable to develop oedema due to salt retention.

The theory of salt-retention as a cause of the oedema possesses several points in its favour which may be worth enumerating. These are:

1. Oedema incidence was restricted to the young age-groups in whom renal function is least efficient.
2. Since cows' milk contains more protein and salt than breast milk, artificially-fed infants have a greater load on their excretory apparatus than breast-fed infants

and thus have a greater tendency to develop renal failure.

3. The subsidence of the oedema (which is a puzzling feature of the condition) may have been due to the patient's return to a normal fluid balance when the cessation of diarrhoea and vomiting allowed the excretion of salt and the release from the tissues of salt-bound water.

It seems likely that impaired renal function is an important factor in the etiology.

Summary and Conclusions

In a series of 176 cases of infantile gastro-enteritis, oedema occurred as a complication in thirty-five (19·6 per cent.).

The preponderant incidence was in the age group under one year, although oedema was noted in patients up to sixteen months.

Spontaneous subsidence of the oedema occurred between two and eight days after onset. In this series oedema never occurred before the fifth day of illness but appeared thereafter, in more than half the cases during the second week of illness, and in almost a third during the third and fourth weeks of illness.

Apart from weight changes which fluctuated parallel with the waxing and waning of the oedema, and from the presence in a few cases of microcytic hypochromic anaemia, there was no other clinical abnormality detected.

The occurrence and duration did not seem to be influenced by the diet. Thus, ' casydrol ' feeds had no effect on frequency and duration of the oedema, and vitamin B deficiency did not appear to be related to the condition.

Comparison of patients treated by sulphonamides with those untreated, indicated that neither sulphaguanidine nor sulphadiazine were related to the production or duration of the oedema.

The death rate in the oedematous patients was 31·4 per cent. (eleven out of thirty-five), and in the non-oedematous, 17·7 per cent. (twenty-five out of 141).

Although a chi-squared test showed that the difference between these death rates was not significant, the chi-squared values were sufficiently close to indicate a tendency for mortality to be higher in oedematous cases than in non-oedematous.

The etiology is obscure, and the present investigation, while enabling the exclusion of some of the possible causes, has not solved this problem. Probably several factors are implicated; of these, the likeliest appear to be: (a) impairment in capillary function; (b) impairment in liver function; (c) impairment in kidney function.

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GIARDIA LAMBLIA

THE INCIDENCE AND RESULTS OF INFESTATION OF CHILDREN IN RESIDENTIAL NURSERIES

BY

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Introduction

Numerous factors exert an adverse influence on the health of children in residential nurseries, of which diarrhoea in its various forms remains the most serious and one of the most insoluble. Apart from the occasional outbreaks of epidemic gastro-enteritis and Sonne dysentery, there is a high incidence of loose stools, and amongst the children who have been at a nursery several months this may take the form of a chronic intermittent diarrhoea. The purpose of this paper is to describe an investigation into the degree of infestation of nursery children with the flagellate protozoon, Giardia lamblia, and to assess its influence not merely in the production of diarrhoea, but on the level of health of the children as shown by failure to gain weight, and by anaemia, poor appetite, etc.

Before the discovery that mepacrine was a specific treatment for Giardiasis (Galli Valerio, 1937), opinions differed widely on the pathogenicity of the organism. Miller (1926) came to the conclusion that Giardiasis was a cause of chronic enteritis in children, but Boeck (1927) gives a rather unconvincing account in support of his belief that Giardia is not pathogenic. Véghelyi (1938, 1940), who has been responsible for much of the later work, considers the three characteristic signs of Giardiasis to be abdominal complaints, anaemia, and retarded development. Steatorrhoea attributable to Giardiasis has been described by Véghelyi (1940), and by McGrath and others (1940). Ormiston and others (1942) reported enteritis associated with Giardiasis in a nursery; and Sudds (1943) reported an outbreak in a nursery school. In both these outbreaks, following treatment with mepacrine, Giardia cysts disappeared from the stools, the diarrhoea ceased, and an improvement was noted in the health of the children.

The Ladywell Nursery

The nursery at which this investigation was carried out is one of the largest and most modern residential nurseries in London. It consists of four separate blocks, and it was intended that each block should be a self-contained unit, except that the food is supplied from a central kitchen. There is accommodation for 156 children up to three years

TABLE 1

ALLOCATION OF ACCOMMODATION: LADYWELL NURSERY

Block	Accommodation	
A	Aged 15-36 months: Ground floor 22	Breast-fed and bottle-fed babies, weaners, and children up to about 15 months: Top floor 20+10 mothers
B	Aged 15-36 months: Ground floor 22	Breast-fed and bottle-fed babies, weaners, and children up to about 15 months: Top floor 20+10 mothers
C	Aged 15-36 months: Ground floor 30	Breast-fed and bottle-fed babies, weaners, and children up to about 15 months: Top floor 20+10 mothers
	[Ground floor C is the admission block for children from 10-12 months up to 3 years. Transferred to other blocks after 2-3 weeks]	
D	Ground floor: Administrative offices, kitchen, etc.	Top floor: 22 (Aged 15-36 months)

of age and thirty mothers, the allocation of the children being as shown in table 1.

On leaving the admission block 'C' the children over one year are transferred to 'D.' On the ground floors of 'A' and 'B' are the long-stay children, aged about fifteen to thirty-six months, that is, those whose stay at the nursery is three months or more, and they are recruited from 'D' when it becomes evident which children are destined to stay long.

Ether concentration method of examination for Giardia lamblia. Direct examination of the stools for Giardia cysts is an unreliable method, and unless repeated examinations are made a large number of cases will be missed. It was therefore decided to use the ether concentration method.

An amount of faeces equal to the size of a large pea is emulsified with normal saline in a 1 oz. screw-cap bottle. A layer of ether is added and the bottle thoroughly shaken. Most of the unwanted debris is taken up in the ether layer. The lower layer of saline containing the cysts and ova is pipetted into a centrifuge tube and spun at 1,500/min. for between five and seven minutes. The supernatant fluid is then discarded and a loopful of the deposit placed on a slide and stained with Gram's iodine; a coverslip is applied.

Details of the Observations

Incidence of infestation with Giardia lamblia. An initial survey involving the examination of one stool from every child in the nursery yielded no positive stools in children under one year. Although a few cases were subsequently found, it was decided that further study of this group was unlikely to yield sufficient information for any conclusive results. All the results given below therefore refer to children aged from one to three years.

INCIDENCE ON ADMISSION TO THE NURSERY. Stools were examined from 139 consecutive admissions over one year of age, two specimens from each child being examined where possible during the first week at the nursery. Thirty-seven out of 139 children (26·6 per cent.) had Giardia cysts in their stools. The difference between the incidence at one to two, and two to three years was not significant ($P\chi^2=0·60$).

The parents were asked whether their children had previously attended a day or residential nursery before their admission to Ladywell Nursery and information was obtained in eighty-six cases (table 2). The difference between the two groups of children (a and b) is significant ($P\chi^2<0·001$). This merely shows that Giardia is more frequently present in children with a history of previous nursery attendance, and it does not prove direct association with nursery life. It is probable, however, that amongst London children in the age group one to three years the incidence of Giardia infestation is somewhat lower than in the 139 children admitted to this nursery.

INCIDENCE IN LONG-STAY CHILDREN. By long stay is meant those children who have been at the nursery three months or more, and since in this nursery the great majority of children on the ground floors of 'A' and 'B' blocks stay this long the incidence of Giardia infestation here may be taken as the incidence in long-stay children. The examinations were carried out during January, 1947. In 'A' block, out of nineteen children, fifteen had Giardia cysts in their stools. In 'B' block, out of twenty children, sixteen had Giardia cysts in their stools (table 3). The low incidence in the age group twelve to eighteen months may be explained by the fact that these children had not long been transferred from the top floors, where the incidence amongst the children up to fifteen months is low. In the case of two of the negative children on 'A' block, one had been positive at the initial survey, and the other positive at a subsequent date. One of the four negative children on 'B' block was later found to be positive. It appears, therefore, that the majority of long-stay children in this nursery are infested with Giardia. Spread of infection probably occurs from child to child by finger and faecal ingestion of cysts, though contaminated dust may be of importance.

TABLE 2

GIARDIA INFESTATION AND PREVIOUS HISTORY OF NURSERY LIFE

History	No. of children examined on admission	Found to be positive	
		No.	%
(a) Previously attended day or residential nursery ..	30	15	50·0
(b) No previous history of nursery attendance ..	56	8	14·3

TABLE 3

INCIDENCE OF GIARDIA INFESTATION IN A AND B BLOCKS ACCORDING TO AGE

Age (months)	Number of children	Found to be positive	
		No.	%
12-18	7	2	29
18-24	15	13	87
24-30	8	7	88
30-36	9	9	100
Total	39	31	79
Over 18 months	32	29	91

INCIDENCE AT OTHER RESIDENTIAL NURSERIES. (a). St. Margaret's Nursery. The great majority at this nursery are destined to be long-stay children, and the rate of admission is consequently low in comparison with Ladywell Nursery. There is accommodation for about eighty children up to three years. Stools were examined from fifty children more than one year old, and in most cases two specimens were examined from each child. Twenty-three out of fifty children (46 per cent.) had Giardia cysts in their stools.

The lower incidence in this nursery may be explained by the fact that there was a larger proportion in the age group twelve to eighteen months (the incidence over eighteen months was 70 per cent.), and by the difference in the type of accommodation. In this nursery the children are segregated into small groups, and as it was formerly an infectious diseases hospital the accommodation is peculiarly suited to this purpose, and there is thus less opportunity for cross infection.

(b.) South-Eastern Hospital Nursery. This consists of two large wards in what was formerly a fever hospital, and each ward holds about twenty-one children. Out of thirteen children over one year of age in one of these wards, eight had Giardia cysts in their stools (61·5 per cent.). Excluding two children who had been at the nursery less than three months, the incidence was 72·7 per cent.

It is evident therefore that the high incidence is not peculiar to Ladywell Nursery and that the majority of long-stay children above one year of age in residential nurseries are infested with Giardia lamblia.

RATE OF INFESTATION WITH GIARDIA AFTER ADMISSION TO THE NURSERY. Stool examination was carried out at monthly intervals during the child's stay at the nursery. It is evident from table 4 that a rapid rate of infestation occurs.

TABLE 4

RATE OF INFESTATION WITH GIARDIA AFTER ADMISSION TO THE NURSERY

Period after admission (months)	Admissions	Number of children negative at previous examinations	Found to be positive		Number remaining negative at end of stated period out of 1,000 admitted negative
			No.	%	
0	139	—	37	26·6	1,000
1		*56	11	19·6	804
2		*15	8	53·3	375

* These are the number of children out of the 139 admissions who were still present in the nursery one and two months respectively after admission. If those positive at one month and again at two months are included, eleven out of eighteen (61·1 per cent.) who were negative on admission were infested at two months.

INCIDENCE IN ADULTS. Stools were examined from the nurses, mothers, and kitchen staff at the nursery. One specimen only was examined in each case. Some difficulty was experienced in getting specimens from the adults, but the figures include all the kitchen staff and about 75 per cent. of the nurses and mothers (table 5). There is clearly no significant difference between the various adult groups, but the overall incidence in adults is significantly lighter than in nursery children. $P\chi^2 = <0{\cdot}00001$.

TABLE 5

INCIDENCE OF GIARDIA IN ADULTS

Group	Number of adults	Found to be positive	
		No.	%
Nurses ..	48	2	4·2
Kitchen staff	9	—	—
Mothers ..	25	1	4·0
Total ...	82	3	3·7

Character of stools and relationship to Giardia infestation. When the specimens of faeces were examined for Giardia cysts a note was made also of their consistency. The following classification was used:

(1) formed stool
(2) semiformed stool } Classed as normal
(3) relaxed stool (which included the intermediate forms between (2) and (3))
(4) fluid stool

It was not possible from the small specimens received to give any satisfactory quantitative estimate for such details as completeness of digestion, presence of mucus, etc.

CHARACTER OF STOOLS OF CHILDREN ON ADMISSION TO THE NURSERY. It was decided to include only those children from whom two specimens had been obtained and from these to take the first specimen only, excluding those from whom the first specimen had been obtained more than seven days after admission. By this means a more accurate picture was obtained of the type of stool on admission to the nursery. Table 6 clearly shows that on admission to the nursery there is no significant stool difference between children with Giardia cysts and those without.

CHARACTER OF STOOLS AND RELATION TO LENGTH OF STAY IN NURSERY. The same procedure was carried out for the stool examinations one month (or more) after admission, and also for the various stool examinations of the children who had been in the nursery for three months or more. The great majority of the latter children were infested with Giardia. It was not considered satisfactory to subdivide the former into Giardia-positive and Giardia-negative because infestation with Giardia might already have occurred although cysts were not yet present in the stools, and it was also difficult to evaluate what other factors were present predisposing to loose stools.

TABLE 6

CHARACTER OF STOOLS ON ADMISSION TO THE NURSERY

(Specimens obtained within seven days of admission)

Whether child positive or negative on admission	Total specimens examined	Stool					
		Normal			Relaxed or fluid		
		No.		%	No.		%
		(1)	(2)		(3)	(4)	
(a) Positive	29	18	8	89·7	3	—	10·3
(b) Negative	81	53	22	92·6	6	—	7·4
Total (a)+(b)	110	71	30	91·8	9	—	8·2

TABLE 7

CHARACTER OF STOOLS AND RELATION TO LENGTH OF STAY IN NURSERY

Time	Total specimens examined	Stool					
		Normal			Relaxed or fluid		
		No.		%	No.		%
		(1)	(2)		(3)	(4)	
(1) On admission ..	110	71	30	91·8	9	—	8·2
(2) One month or more after admission ..	145	51	54	71·0	26	14	27·6
(3) Long-stay children (excluding cases who had taken mepacrine)	162	68	54	75·3	28	12	24·7

The differences between (1) and (2) and between (1) and (3) in table 7 are significant. $P\chi^2 = <0{\cdot}001$ in both instances.

Loose stools are more frequent in these nursery children. The type of stool passed by children after a long stay in the nursery is more strikingly different than is suggested by the above figures, and interestingly aperients in residential nurseries of this type are rarely required. On admission a brown, well-formed stool is usual; but this emphatically is not the case in the long-stay child, with whom the average stool tends to be rather grey in colour, and of greasy appearance, although its consistency may be within normal limits. The undigested stool is also common, and excess mucus may be noticeable in some of these.

The relationship of height, weight, haemoglobin percentage, and faecal fats to Giardia infestation.

WEIGHT AND HEIGHT OF NURSERY CHILDREN AND RELATIONSHIP TO GIARDIA INFESTATION. Some difficulty was experienced in obtaining a suitable standard for heights and weights of children between one and three years. No standard was available for nursery children or even for children of this age group in the London area, so the one finally used was an accepted American standard compiled from the University of Iowa Studies in Child Welfare (Meredith, H. V., 1935, and Boynton, B., 1936, and quoted in Mitchell-Nelson's 'Textbook of Paediatrics').

As this is a standard for American children it was decided that the weights and heights of a group of healthy British children should be obtained for comparison, before applying the standard to the nursery children. For this purpose the heights and weights of children of this age group (one to three years) attending a local infant welfare clinic were obtained, and the results were as shown in table 8.

The weights of these children attending the infant welfare clinic compare favourably with the standard, but it seems that the standard for heights is rather high for the average London child of this age group.

(a.) Weights and heights on admission to the nursery. The children were divided into those who had Giardia cysts in their stools on admission and those who had not (table 9).

The differences between the actual and expected mean height and weight of those children who were Giardia infested on admission are somewhat greater

than that of the children who were Giardia-negative on admission, but the differences between the two groups for both heights and weights are not statistically significant. As was mentioned previously, a greater proportion of Giardia-positive children had previously attended a nursery, and this may be a factor accounting for the small differences between the two groups.

(b.) Weights and heights in long-stay children. The weights of fifty-two children and the heights of forty children who had lived in the nursery for three months or more were obtained. It was desirable to know whether these children who were destined to stay long were inferior to the average admission child. Thirty-six long-stay children who were over one year of age on admission to the nursery were taken, and their weights on admission and later were recorded in table 10. The expected heights and weights are the mean of individual expectations according to the standard used.

The conclusions to be drawn from table 10 are:

1. The longer a child remains at this nursery the more subnormal he becomes.
2. The average child on admission to the nursery is inferior both in height and weight to an average child attending a local infant welfare centre. This is to be expected because the conditions necessitating admission to a residential nursery are often similar to those having an adverse influence on the physical health of a child.
3. A child, after admission to a large residential nursery, does not show an improvement as might be expected, but becomes gradually more subnormal.

TABLE 8

HEIGHT AND WEIGHT OF CHILDREN AGED ONE TO THREE YEARS ATTENDING AN INFANT WELFARE CLINIC

Number weighed	Mean weight (lb.)			Number measured	Mean height (in.)		
	Actual	Expected*	Difference		Actual	Expected*	Difference
88	29·17	29·08±0·32	+0·09	30	34·12	34·99±0·22	—0·87

* Expected = means of individual expectations according to the standard.

TABLE 9

WEIGHT AND HEIGHT ON ADMISSION AND RELATIONSHIP TO GIARDIA INFESTATION

Giardia cysts on admission	Number weighed	Mean weight (lb.)			Number measured	Mean height (in.)		
		Actual	Expected*	Difference		Actual	Expected*	Difference
Present ..	37	24·67	27·20±0·48	—2·53	34	31·69	33·64±0·20	—1·95
Absent ..	99	25·30	27·11±0·29	—1·91	81	32·01	33·62±0·13	—1·61

* The expected heights and weights are the means of individual expectations on the standard used.

TABLE 10

HEIGHTS AND WEIGHTS OF CHILDREN ON ADMISSION TO THE NURSERY AND AFTER THREE MONTHS OR MORE

Group	Number weighed	Mean weight (lb.)			Number measured	Mean height (in.)		
		Actual	Expected	Difference		Actual	Expected	Difference
On admission (from table 9)	136	25·06	27·13±0·25	—2·07	115	31·92	33·63±0·11	—1·71
Long-stay children	52	25·62	28·64±0·42	—3·02	40	31·37	34·56±0·19	—3·19
Long-stay children over 1 year on admission:								
(a) on admission	36	24·73	26·97±0·48	—2·24				
(b) after 3 months or more ..	36	27·06	29·72±0·52	—2·66				

HAEMOGLOBIN OF ADMISSION AND LONG-STAY CHILDREN. This was determined by the Haldane method, using for comparison a B.S. tube No. 1079 (table 11). Age for age there is no significant difference between the two groups. Of ten admission cases with haemoglobin less than 70 per cent., three were positive for Giardia, and of four long-stay cases with haemoglobin less than 70 per cent., three were positive for Giardia. In neither case is this significantly different from expectation for all admissions or long-stay children respectively, regardless of haemoglobin.

TABLE 11

HAEMOGLOBIN OF ADMISSION AND LONG-STAY CHILDREN

Group	Age (months)	Haemoglobin			
		< 70%	70-80%	80% and over	Total no. of children
On admission	12-18	3	17	14	34
	18-24	3	14	17	34
	24-30	3	4	14	21
	30-36	1	5	5	11
	Total	10	40	50	100
Long-stay	12-18	—	1	4	5
	18-24	4	6	7	17
	24-30	—	2	5	7
	30-36	1	4	8	13
	Total	5	13	24	42

THE FAECAL FATS OF A GROUP OF LONG-STAY CHILDREN. Steatorrhoea has been described as occurring in cases of heavy infestation with Giardia lamblia (Véghelyi, 1940). The greyish, rather greasy stools which are so commonly found in residential nurseries suggested that a high fat content in them might be expected. A group of fourteen was selected from the long-stay children, Giardia infestation having been found in thirteen of them. All these children were below expected weight according to the standard, muscle tone was poor, and they had a history of loose stools at some time during their stay in the nursery, and many of them a history of intermittent diarrhoea. The clinical picture presented by these children resembled quite well that which has been described as due to Giardia infestation. In all cases the faecal fats were within normal limits, although two cases were a little high (total fat 34·4 and 37·6 per cent. respectively). The mean of the fourteen cases was total fat per cent. $25 \cdot 35 \pm 1 \cdot 89$, split fat $22 \cdot 51 \pm 1 \cdot 80$, unsplit fat $2 \cdot 84 \pm 0 \cdot 30$.

The food intake of these children was also measured. From the nutritional aspects the intakes appeared to be ample, and the total fat per twenty-four hours tended perhaps to be rather on the high side of the optimum. It did not appear, therefore, that steatorrhoea was a manifestation of Giardia infestation in this nursery.

The effects of treatment with mepacrine.

MEPACRINE TREATMENT—EFFECT ON GROWTH. As previously mentioned, the great majority of the children on the ground floors of 'A' and 'B' blocks were long-stay children between the age of fifteen months and three years with a very high incidence of Giardia infestation. They were therefore eminently suitable for a study of the effect of Giardia infestation and results of treatment (table 12). Regarding the absolute physique of the two groups, that part of the difference which is not accounted for by age is well within the range of sampling error, and the two groups may be regarded as comparable.

TABLE 12

ABSOLUTE MEASUREMENTS ON A AND B: FEBRUARY, 1947

Block	No. of children	Average age (months)	Mean weight (lb.)	Mean height (in.)
A	16	25·7	$25 \cdot 94 \pm 0 \cdot 97$	$31 \cdot 8 \pm 0 \cdot 6$
B	17	23·6	$24 \cdot 32 \pm 0 \cdot 82$	$30 \cdot 9 \pm 0 \cdot 5$
Difference ..		2·1	1·62	0·9
Expected difference on basis of age			0·86	0·7
Difference not explained by age			0·76	0·2

It was decided to treat the children on 'B' block with mepacrine and to use those on 'A' block as controls. Mepacrine treatment was started on 'B' in the middle of February and all the children in this group received it. The mepacrine was given in the form of 0·025 g. tablets, and children under eighteen months were given 0·075 g. daily and those over eighteen months 0·1 g. daily, the course lasting five days. No toxic symptoms were observed, although a few children developed a yellow colour of the skin, but in no case was this marked.

Examination of the stools a few days after treatment showed that there was complete elimination of Giardia cysts from the stools. Stools from all the children treated with mepacrine were subsequently examined at monthly intervals until the end of June, and in no case were any Giardia cysts demonstrated during the period of survey. All children subsequently admitted to this block received a course of mepacrine before mixing with the other children. Mepacrine thus provides a simple and reliable method for the elimination of Giardia infestation.

A record had previously been obtained of the gain in weight per week of long-stay children on

'A' and 'B' blocks during the period October, 1946, to February, 1947; comparably the mean gain in weight and height on 'A' and 'B' during the period of survey were obtained, and are shown in table 13. There is no significant difference between the rates of weight gain of the children in the two blocks before treatment, and there is no significant difference between the rates of weight gain of the control group in the two periods. The rate of gain of the mepacrine group during the period after treatment is significantly higher than before treatment and higher than that of the control group. The difference in height gain between the controls and the treated group is $0{\cdot}024 \pm 0{\cdot}014$, which is barely significant.

TABLE 13

GROWTH-COMPARISON BETWEEN CHILDREN ON A AND B BLOCKS BEFORE AND AFTER MEPACRINE

Period	Group	No. of children	Mean gain per week	
			Weight (oz.)	Height (in.)
Oct., 1946 to Feb. 1947	A	21	$1{\cdot}52 \pm 0{\cdot}28$	
	B	21	$1{\cdot}16 \pm 0{\cdot}21$	
Feb. 1947 to June, 1947	A (controls)	21	$1{\cdot}54 \pm 0{\cdot}24$	$0{\cdot}079 \pm 0{\cdot}009$
	B (mepacrine)	21	$2{\cdot}79 \pm 0{\cdot}22$	$0{\cdot}103 \pm 0{\cdot}010$

During the period of survey, bacteriological examination of the stools from 'A' and 'B' blocks did not reveal any pathogenic organisms. There was an outbreak of whooping-cough on 'B' block at the end of February and during March. Five cases occurred during this period, and there were one or two suspicious cases which were not confirmed. It is possible that, but for this unfortunate occurrence, the difference between 'A' and 'B' would have been even more marked. There were no other serious diseases on these blocks during this period.

LOOSE STOOLS ON 'A' AND 'B' BEFORE AND AFTER MEPACRINE. For this purpose a record was made of the number of days on which a child was reported by the sister-in-charge as having loose stools. The information is necessarily incomplete, because owing to the frequent occurrence of loose stools in this nursery the first loose stool may not be reported and subsequently may not be mentioned throughout the period of the diarrhoea. An attempt was made to obtain a complete record of the number of stools passed per day by each child on these two blocks, but this proved impossible. The former method was applied for the period from the beginning of mepacrine treatment on 'B' block in February until the end of May, and also for a similar period on 'A' and 'B' blocks (three and a half months) prior to the use of mepacrine.

No dramatic results were observed during the first week or two after the use of mepacrine on 'B' block. This accords with the view of Véghelyi (1940), who considered that recovery took from three and a half to seven weeks after treatment. But during the subsequent months it was unquestionably evident that the incidence of loose stools on the treated block was less than on the control block (table 14).

TABLE 14

LOOSE STOOLS AND/OR VOMITING REPORTED ON A AND B BLOCKS

Period	A Block		B Block	
	Total reports*	No. of children involved	Total reports*	No. of children involved
Nov. 1, 1946, to Feb. 14, 1947 ..	176	22	123	24
Feb. 14, 1947, to May 31, 1947	127	21	40	12
April and May, 1947	75	19	10	7
Loose stools only during April and May, 1947	72	18	4	3

* Total reports = No. of occasions (24-hour period) children were reported as having loose stools and/or vomiting.

During the period November 1, 1946, to February 14, 1947, taking into consideration admissions and discharges, there was a total of thirty-five children on 'A' and thirty-eight children on 'B' blocks. For the period February 14 to May 31 the corresponding figures were twenty-nine children on 'A' and thirty-two on 'B,' so that the number of children 'at risk' on the two blocks is therefore comparable.

HAEMOGLOBIN BEFORE AND AFTER TREATMENT. The haemoglobin of each child on 'A' and 'B' was estimated at the end of January and again at the beginning of June. There was some improvement in the haemoglobin of the children in 'B' block after treatment with mepacrine, but as the two groups ('A' and 'B' blocks) were not strictly comparable as regards level of haemoglobin in January it was not possible to assess how much of this improvement could be attributed to the elimination of Giardia lamblia. Unfortunately in a nursery of this type it is not possible to compare treated and control groups over a period longer than a few months as there is constant wastage from children returning home, being adopted, etc.

OTHER EFFECTS ON THE HEALTH OF THE CHILDREN ON 'B.' It was difficult to assess the effect of mepacrine treatment on appetite and muscle tones. Muscle tone was poor in the majority of these

long-stay children when the investigation began; and in June, when the children were able to get plenty of fresh air and sunshine, the general conditions of both groups 'A' and 'B' had improved, but possibly 'B' showed greater improvement. For the most part the appetites of the children on both 'A' and 'B' were good, and there was no obvious change following mepacrine.

TREATMENT OF 'A' BLOCK WITH MEPACRINE. At the beginning of June all the controls on 'A' block were given a five-day course of mepacrine. During the subsequent month there was a definite improvement, both as regards incidence of loose stools and rate of weight gain. It was not possible, unfortunately, to continue observation of the individual children on 'A' and 'B' after the beginning of July. Many of the original children had already been discharged, and of those remaining some were due for transfer to nursery schools. Further, it had been decided to rearrange the accommodation of the nursery and it was no longer practical to have two comparable groups of long-stay children.

Relationship of Giardia infestation to the onset of diarrhoea. During the period of survey nineteen children who were negative on admission became infested with Giardia a month or more later. Two of these children were admitted to hospital. Only one appeared ill at the time of admission to hospital; the other, who had had Giardia cysts in the stools for some weeks, had blood in the stools and clinically suggested a case of Sonne dysentery (history of Sonne dysentery twice before), but repeated stool examinations failed to confirm this. In the other cases there appeared to be no relationship between the occurrence of Giardia cysts in the stools and the onset of diarrhoea, and in three of the cases who became infested no loose stools were reported.

After admission to the nursery a record was kept of the number of occasions (twenty-four-hour period) that a child was reported for loose stools. The results obtained for the first five months of 1947 showed that loose stools were about as frequent in the children who remained negative as in those who became positive. The majority of the children in this group were short-stay children, that is, they were at the nursery less than three months.

During the period of investigation eight children over the age of one year at Ladywell Nursery were sufficiently ill with diarrhoea to be admitted to hospital. Two of these had Giardia cysts in their stools and have been mentioned above. Two of the remainder were involved in an outbreak of severe enteritis on the admission block 'C,' four cases being admitted to hospital (two of them only ten months old), and there were two deaths. The onset was acute, with diarrhoea, vomiting, and marked prostration, and no outbreak of such severity had been seen amongst children of this age group in the previous twelve months. The cases occurred within a few days of one another, and there appeared to be no evidence that Giardia was in any way connected with this outbreak. No evidence of Giardia infestation was found in the remaining four children in spite of repeated examinations which included examination for flagellates of fresh stools and duodenal fluid. Bacteriological examination failed to find any pathogenic organisms, and administration of sulphasuxidine was without effect. No evidence of parenteral infection was found. Recovery was slow but uneventful, and it was two or three weeks before the children's appetites became normal.

Discussion

It has been shown that there was a very high incidence of Giardia infestation among long-stay children in residential nurseries, and that there was a higher incidence of loose stools in these children than in children on admission to the nursery. There was, however, no significant difference between the heights, weights, and character of stools of children who had Giardia cysts in their stools on admission to the nursery and those who had not. A follow-up of children during their first few weeks or months of nursery life showed that loose stools were about as frequent in those who remained free of Giardia infestations as in those who became positive. This suggests that factors other than Giardia infestation are of primary importance in explaining the higher incidence of loose stools amongst the nursery children.

It is not possible in this short paper dealing primarily with Giardia lamblia to discuss fully the various other factors leading to diarrhoea and failure to thrive in residential nurseries. Dietetic and psychological disturbances are undoubtedly factors predisposing to diarrhoea during the first few weeks at a nursery, but infections of various kinds, especially upper respiratory, are probably the most important factor. In this nursery, apart from the admission block, there are twenty to twenty-two children on each floor, sharing the same playroom, dining room, bathroom, and potting room. The high incidence of infection during a child's first year at school is well known and in a nursery the child is exposed to the same risks of multiple cross infection at an age when he is less in condition to withstand them. The risks of infection can be overcome to some extent by keeping the children in small groups and allowing them to mix only when out of doors. This method had been adopted on the admission block 'C,' but the accommodation on the other blocks was not suitable for the purpose.

Many of the children had loose stools on returning home, but these returned to normal after a period varying from a few days to several weeks without treatment with mepacrine. Furthermore, in no case

did the parents admit that a child suffered from chronic intermittent diarrhoea as a result of past attendance at this or any other residential nursery. Elimination of Giardia infestation by treatment of a group of long-stay children with mepacrine was followed, however, by a marked improvement in their general health, as shown by the gain in weight and decrease in incidence of loose stools. These apparently contradictory facts together with those previously mentioned can be explained on the assumption that conditions giving rise to a chronic dyspepsia or leading to other forms of intestinal disturbance pave the way for Giardia to assume a pathogenic role. Under these conditions infestation with Giardia leads to the occurrence of intermittent diarrhoea and failure to thrive, although it is probable that a stay of several weeks or months is necessary for this to occur and it thus assumes greater importance in the long-stay child. Whilst such a child remains in the nursery an improvement in his health may be obtained by elimination of the Giardia. If, however, the child returns home it is possible that having thereby removed all the many adverse influences exerting their effect on the nursery child, gradual recovery may occur without removal of the Giardia which assumes a more minor role as the condition of the bowel and the general health of the child improve.

Summary

1. The incidence of Giardia infestation on admission to the nursery in children from one to three years was 26·6 per cent. There was no significant difference in the incidence of infestation between the age groups one to two, and two to three years.

2. From a group of eighty-six of these children, thirty had previously attended a day or residential nursery. The incidence of Giardia infestation in these children was 50 per cent., but the incidence in fifty-six children who had not previously attended any nursery was only 14·3 per cent.

3. The great majority of the long-stay children over one year old at this nursery were infested with Giardia. In a random group of long-stay children the figure reached 79 per cent., and this high figure is in agreement with results obtained at other nurseries. Under the age of one year the incidence of Giardia infestation is low.

4. There was a rapid rate of infestation with Giardia after admission. Of those children who were negative on admission, about two-thirds were infested at the end of two months.

5. The incidence in adults at this nursery was 3·7 per cent. on one examination. Other cases were later found, but the overall incidence was significantly lighter than in nursery children in general.

6. (i) The average child admitted to the nursery was on admission inferior both as regards height and weight to an average child attending the local infant welfare clinic. (ii) The children on admission to the nursery were superior both as regards heights and weights to the children who had been at the nursery for three months or more. (iii) The children who had been at the nursery three months or more were not, when they were admitted to the nursery, inferior to the average child admitted.

7. There was no significant difference in height and weight between children who had Giardia cysts in their stools on admission and those who had not.

8. Loose stools were more frequent in children who had been at the nursery for several weeks than in children just admitted.

9. On admission there was no significant difference between the stools of a Giardia infested child and those of a child not infested.

10. The inference to be drawn from 7 and 9 is that some factors other than Giardia must play a part in accounting for the difference between children on admission to the nursery and those who have been there several months or more. The importance of other factors such as dietetic upset, infections, and psychological disturbances has been mentioned.

11. No significant difference was found between the haemoglobin percentage of the long-stay nursery child and that of children on admission.

12. There was no evidence of any marked inability on the part of the Giardia-infested children to absorb fats.

13. The group of Giardia-infested children treated with mepacrine showed a significantly greater rate of weight gain than the control group of children. The results also suggested that the increase in the height and the haemoglobin percentage of the treated group would have shown a significant improvement over the controls had a longer period of survey been possible. There was a marked decrease in the incidence of loose stools among the treated children.

14. The improvement following mepacrine was a gradual process such as might be expected to occur in a chronically inflamed intestine which would take some time to return to normal.

15. There appeared to be no definite relationship between the occurrence of Giardia infestation and the onset of loose stools. Dietetic upset, infections, especially upper respiratory, and psychological disturbances are probably the important factors predisposing to the onset of diarrhoea after admission to the nursery.

16. There was no evidence to support the view that severe cases of non-specific enteritis can be attributed to Giardia lamblia. The suddenness of such outbreaks and the rapidity of spread to other children suggests a bacterial or virus cause.

17. The role of Giardia lamblia as a factor in diarrhoea and failure to thrive in residential nurseries has been discussed.

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ERB'S PALSY

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The term Erb's palsy is applied to that particular type of birth palsy in which the paralysis, or paresis, is confined to muscles supplied by the fifth and sixth cervical nerves. The deltoid, supra-spinatus, infra-spinatus, teres minor, biceps, brachialis, brachio-radialis, and supinator muscles are usually involved in severe cases, whereas in mild cases only some of these muscles are affected. As a result of the paralysis of the above muscles, the attitude of the arm affected by Erb's palsy is characteristic and follows logically on the lack of power in the paresed or paralysed muscles, that is, the arm hangs inert by the side as a result of lack of power in supra-spinatus and deltoid ; the elbow is extended as a result of involvement of the elbow flexors; the hand is rotated so that the palm faces backwards, resulting from the unopposed pull of sub-scapularis and loss of power in the supinator and brachio-radialis. There are no sensory changes.

The palsy is now usually accepted as being due to stretching of the supra-clavicular portion of the brachial plexus during birth, and therefore obstetrical technique is a main factor in considering the etiology.

Apart from a report on 150 selected cases by Sever (1916), a search of the literature has failed to reveal any other large series of these cases, and it was felt that useful information about the condition and the results of treatment could be elicited by reviewing the cases which have attended the out-patients' department of this busy provincial teaching hospital during the last twenty-one years. Actually 125 cases of Erb's palsy presented themselves during that time, but the author has only been successful in tracing and interviewing thirty-seven of this group. For the purpose of studying the incidence of the condition, the whole series of 125 cases has been reviewed. In discussing the effect of treatment, only the thirty-seven cases followed up have been considered.

Incidence

Of the 125 cases sixty-six occurred in male children, and fifty-nine in female, a sex incidence very slightly in favour of males. Sixty-eight cases showed a left-sided palsy, and fifty-three showed a right-sided palsy, while four were bilateral. At the time of review the ages of these cases varied from 2 years 1 month to 25 years.

Birth Details

As birth injury is accepted as a causative factor, it was not surprising to find that fifty-four cases occurred in primigravida, while twenty-nine cases were second children. Subsequent pregnancies accounted for forty-two cases. It is interesting to note, however, that the paralysis occurred in a fifteenth child, a breech birth with extended arms, and also in a sixteenth child, a vertex presentation delivered without forceps.

Moreover, it was found that ninety-one cases were delivered as vertex presentations, and in forty-seven of these forceps were used to assist delivery. (In the thirty-seven cases reviewed, four mothers particularly stated that there had been trouble with delivering the arm or shoulder, but such details could not be obtained in other cases.) Of thirty-two breech presentations, eleven necessitated the use of forceps. Thus forceps were used in approximately half the number of deliveries, and the part played in causation of palsy is problematical. Sever's experiments on the cadaver suggest that lateral bending of the head and neck to the opposite side causes injury to the fifth and sixth cervical nerves, and the vigorous use of forceps may be an etiological factor in these cases. In addition, there is more likelihood of causing injury to the brachial plexus and subsequent Erb's palsy in delivering the arms in a vertex presentation than in a breech presentation.

However, by far the most striking factor noticed was the large size of the babies at birth. Apart from two average cases weighing 7 lb., two weighing 6¼ and 6½ lb. respectively, and one weighing 5 lb., all other cases weighed 8½ lb. or over, several weighing 10, 11 or 12 lb. while one weighed 13 lb. and another actually 16 lb. The average weight for the series was 11½ lb. Presumably a big baby causes greater trouble in delivery, particularly in bringing down the arms if they are caught above the head.

Treatment: Thirty-seven Cases

The treatment of all cases was that of adequate splintage associated with massage, together with exercises in older children. A simple abduction

TABLE
ANALYSIS OF TREATMENT OF THIRTY-SEVEN CASES OF ERB'S PALSY

Treatment started	No. of cases	Completely recovered	Length of treatment (years)	Failures	Length of treatment (years)
Under 1 month	13	12	2	1	4
At 1 month	5	2	¾	3	2
„ 2 months	8	3	1	5	1
„ 3 „	1	0	—	1	3½
„ 4 „	2	0	—	2	2½
„ 5 „	1	0	—	1	7
„ 7 „	1	0	—	1	2
„ 9 „	1	0	—	1	2
Over 1 year	4	0	—	4	2
„ 4½ years	1	0	—	1	2

light metal splint was used with the shoulder abducted and externally rotated, the elbow flexed at a right angle and the forearm supinated. By hanging coloured balls over the cot or pram, active movements were encouraged early. The average length of treatment seems to have been about two years, although many cases achieved complete recovery in much less than this period, while several unrecovered cases had longer treatment. Treatment was started at varying intervals after birth. In some cases it was not started till late, as the diagnosis was missed in the early stages, and in other cases the parents were told that no treatment could be given till the baby was older. Unfortunately, the main difficulty which militates against successful treatment is the early development of contractures in the unaffected muscles of the arm, resulting in deformities and loss of power to carry out essential movements.

Cases have been divided into groups according to the age when treatment was initiated. It can be immediately seen that the age when treatment was started plays an important part in the final result of the case.

Group 1. Cases treated under one month of age. It can be seen from the table that twelve out of thirteen cases treated before they were one month old recovered completely, although one of these cases subsequently (ten years later) developed a crippling scoliosis. The only failure in this group was one right-handed case that was unfortunately neglected while under treatment. Failing to attend for massage and passive movements, he developed a stiff shoulder and elbow while splinted in the second position. This necessitated subsequent manipulation and has left him with a wasted deltoid, impaired abduction and internal rotation of the shoulder, and limited pronation. He is now using the left hand for all purposes.

Group 2. Cases treated at one month and later. Out of five cases, in only two was a complete recovery obtained. In the other three cases although treatment was prolonged, in one case as long as twelve years, severe disability remains. Two cases in this group needed division of the right pectoralis major tendon to alleviate adduction deformity. In no case was it found necessary to divide the subscapular tendon as advised by Sever.

Group 3. Cases treated at two months or later. Out of eight cases, three only showed a complete functional recovery, although two of these cases revealed some wasting of the deltoid muscle on the affected side compared with that on the other.

Results of late treatment. Cases where treatment was commenced at three months or later invariably did badly. Apart from group 1 cases, and two complete recoveries in group 2, all other cases showed impaired function. The moral from this analysis is that treatment must be carried out from birth. It is wrong to say, 'Wait till the baby is older.'

At the shoulder abduction was limited in all cases so that the arm could not be raised beyond a right angle in the milder cases, whereas in the severe cases 30 degrees of abduction only was possible. In these cases there was a varying degree of wasting of the deltoid muscle, and it was frequently stated that work was only possible as long as it could be carried out below shoulder level. External rotation was also limited; in fact, wasting and contracture of the subscapularis led to internal rotation deformity. Thus, the eight right-hand cases in this category were unable to comb the hair and have become left-handed for all common purposes.

At the elbow extension was limited in four cases, while in three there was limitation of supination movement to the mid-position only.

The handgrip remained unaffected in all unrecovered cases.

One case in group 9 was associated with severe mental defect. This child, birth weight 7¾ lb., a vertex presentation on delivery without forceps,

was only noticed to have a palsy at six months, and did not commence treatment till one year old. He was late in sitting up and walking, and at the time of examination at the age of 3 years 3 months, was subject to fits and continual screaming attacks.

Thus as a result of late treatment, contractures develop in four main groups: (1) sub-scapularis, leading to internal rotation deformity; (2) pectoralis major, leading to adduction deformity; (3) pronator teres, leading to pronator deformity at the elbow; (4) flexion deformity at the elbow.

Various operative methods have been devised to correct the contracture deformities (Meehan, 1940), but in this series of thirty-seven, apart from division of the pectoralis major tendon in two cases, it was felt by the surgeon-in-charge (R. Ollerenshaw, M.D., F.R.C.S.) that no benefit could be gained by surgical interference in the other cases.

Summary

1. End result of thirty-seven cases of Erb's palsy have been investigated.

2. The condition is slightly more common in males.

3. Injury at birth to the supraclavicular portion of the brachial plexus is the accepted cause of the condition, and therefore, skilled obstetric technique in delivery, particularly in the use of forceps, is the main factor in avoiding this paralysis.

4. Large babies are more likely to be injured. A large child in a primigravida needs very special care with the delivery of the head and arms.

5. Treatment must be carried out from birth. Cases treated within the first month do uniformly well and results are 100 per cent. successful.

6. If treatment is delayed, contractures causing impaired function of the shoulder and elbow will develop very quickly.

My thanks are due to Mr. R. Ollerenshaw, M.D., F.R.C.S., for helpful criticism and advice, and for allowing me full access to his cases.

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CASE REPORTS

TWO CASES OF CONGENITAL DISEASE OF THE HEART WITH SUB-DIAPHRAGMATIC SITUS INVERSUS

BY

R. H. HARDY, B.M.

(From the Children's Department, University College Hospital, London)

The two rare cases to be described, which happened to be sent to this department within a few months, are worth recording both for their own interest and as an addition to the scanty literature relating to this unusual syndrome. It is also of interest that in both cases the diagnosis was not at once apparent, although all the necessary information was readily available on examination.

Case Histories

Case 1. A male, aged 9 months, had always been healthy and normal in development. During routine attendance at a child welfare centre the doctor noticed that he was cyanosed and sent him to a hospital, where a diagnosis of respiratory embarrassment due to an enlarged thymus was made. The child was sent to University College Hospital, where further investigations were carried out.

PHYSICAL EXAMINATION. A well developed, plethoric child showed cyanosis of lips, fingers, and toes, and moderate clubbing of fingers and toes. There was no dyspnoea or stridor. The weight was 17½ lb.

The heart was in the normal position, slightly enlarged to left, with a loud systolic murmur over the praecordium; the maximum murmur was at the pulmonary area. The lungs were normal. The liver was symmetrically palpable. All other systems were normal.

RADIOGRAPHY. The chest radiograph showed the heart enlarged to left with very prominent pulmonary conus. The liver shadow was symmetrical (fig. 1).

Barium swallow. Barium was seen in the oesophagus, passing to the right through the diaphragm and outlining a normal stomach and duodenum in the mirror-image position.

Barium enema. The sigmoid and descending colon were in the right iliac fossa.

ELECTROCARDIOGRAPH. This showed simple sinus tachycardia, abnormal Q.R.S. complex, and large S wave in all three leads, and large P and T waves in Lead II (fig. 2).

FAMILY HISTORY. The parents and their relatives are normal. There is one male sibling surviving; he is normal and aged eleven years. The mother had had one stillbirth in 1933, a baby with bilateral talipes. There had been no post-mortem examination.

Case 2. A female, aged 17½ months, had been apparently normal and healthy up to the age of 12 months, when she ceased to gain weight. The parents had noticed blueness of the lips on several occasions, especially when the child cried or coughed. She was taken to a hospital, where a diagnosis of tuberculous hilar adenopathy with pulmonary congestion was made on the radiographic findings and history of four weeks' cough. She was then transferred to University College Hospital where further investigations were made. A history of pertussis contact was later elicited.

PHYSICAL EXAMINATION. The child was small, thin, and pale, with blue lips, and rapid pulse and respiration rates. She had repeated bouts of coughing. She was normally intelligent and co-operative. There was early clubbing of the fingers. The weight was 16 lb.

The heart was in the normal position, enlarged to right and left, with no murmurs.

There were widespread rhonchi and crepitations in the lungs, more on the right side than on the left. A slightly enlarged and soft liver was palpable in the left hypochondrium. All other systems were normal. The Mantoux reaction was negative.

RADIOGRAPHY. A radiograph of the chest showed the heart enlarged to both sides, a prominent pulmonary conus, and congestion of both lung fields spreading from the hilum. There was a stomach bubble under the right dome of the diaphragm, with the liver shadow under the left (fig. 3).

After a barium meal the position of the stomach was confirmed; the duodenum was not clearly outlined but was probably in the mirror-image position; the caecum was in the left iliac fossa, the descending colon and sigmoid in the right.

ELECTROCARDIOGRAPH. This showed simple sinus tachycardia. There were substantially normal curves with flat T wave in all leads and inverted P in Lead III (fig. 4).

FAMILY HISTORY. The parents are normal. There is one female sibling, normal, and aged four and a half years; and one male sibling, normal, and aged three months. A paternal aunt has a deformed hand, the fingers being only half an inch long, and a paternal cousin congenital absence of the right foot and deformity of one hand.

Review of the Literature

The literature on visceral heterotaxy is extensive, but particular reference must be made to Lichtmann's (1931) thorough review of the subject in its relation to heart disease. In brief, the incidence of situs inversus with this association may be summarized from the available literature of the last fifteen years as follows:

1. Total situs inversus with mirror-image dextrocardia giving rise to no abnormality is relatively common.
2. Total situs inversus with congenitally abnormal dextrocardia is not unduly rare. Six cases picked at random showed three instances of Eisenmenger's complex, one of Fallot's tetrad, and two of functionally bilocular heart with persistent conus arteriosus.
3. Partial situs inversus with normal laevocardia is uncommon; eight cases in all were recorded, mostly chance findings in otherwise healthy subjects.
4. Isolated dextrocardia is rare, but, when it occurs, is usually associated with congenital abnormality. In Lichtmann's series of 161 cases, only three showed a normal heart.
5. Partial situs inversus with congenitally abnormal laevocardia (the condition under discussion) is also rare. Diligent search has brought records of seven cases to light, the description of one of which (Clemente, 1931) is not available in this country. The case recorded by Shaw and Blake (1924) is not felt to be a true instance of this syndrome because they obtained the electrocardiograph typical of dextrocardia, while the clinical position of the heart appears from their evidence to have been at least central.

Developmental Aspects

Cockayne (1938) suggests that situs inversus is a Mendelian factor carried by a recessive autosomal gene, and has therefore a definite familial incidence in families where consanguineous matches have occurred. He cites the frequent association of other congenital abnormalities, particularly heart disease, and mentions the association of congenital bronchiectasis, and paranasal sinusitis with situs inversus—Kartagener's triad (Kartagener, 1933; Kartagener and Ulrich, 1935). He also suggests that in partial situs inversus the frequency of congenital morbidity is higher than in complete. He explains the partial type on the basis of an 'allelomorphic' gene.

The embryological account of the matter refers to the failure of completion of the normal 'embryonic spiral' in which the abdominal and thoracic organs migrate from their early median positions to their normal adult-situations. Abbott (1936) refers to the arrest of development of the heart at a stage bearing an atavistic resemblance to reptilian or amphibian types, as in the case of bilocular and trilocular hearts with persistent right-sided aorta.

In an article which is the only critical review of this subject Forgacs (1947) goes into the embryological aspect of the question more fully and gives a most convincing account of the condition's development. For practical purposes, he believes, when the heart is on the same side as the liver it is never free from congenital morbidity.

In the two cases here described there is no suggestion of consanguineous marriage for three generations and no evidence of situs inversus in any near relations. The incidence of the other types of congenital deformity in relatives of Case 2 is, however, of some interest.

Diagnosis

Although it is almost impossible to draw any conclusions, it is perhaps relevant to mention the six other cases of which records are available. Of the three who came to post-mortem examination all had transposition of the aorta and pulmonary artery with left-sided aortic arch; all three had patent interventricular septa—two with small openings and loud systolic murmurs, one with almost complete absence of the septum and no murmur; two had atresia of the pulmonary artery with persistent ductus arteriosus; all were cyanotic and dyspnoeic on effort.

Added to these facts, Abbott has a radiograph in her atlas of a case of transposition of the great vessels with defective interventricular septum; there is enlargement of both ventricles and prominence of the pulmonary conus remarkably similar to that shown in our two cases.

Neither of Forgacs's cases had come to autopsy.

Prognosis

It is possible to say only that one child looks fit and the other far from it. Of the six similar cases, one was alive at nine years (Girod and Sarasin, 1932) and another died at nineteen years (Pernkopf, 1928). The others lived only for ten weeks (Miller, 1925) and seven months (Hu, 1929). Of Forgacs's cases, one was alive and fit at 25 years, the other less fit at five years. Abbott's case of transposition of the great vessels with defective septum also had complete heart block and lived until the age of twenty years.

Conclusion

It seems fair to infer from the rather scanty evidence that partial situs inversus tends to be associated with gross abnormalities of the heart of a type which can be accounted for theoretically by disorders of the 'embryonic spiral.' It is not

FIG. 1.—Case 1: radiograph showing heart in normal position, with enlarged pulmonary conus. A stomach bubble can be seen overlying the right lobe of the symmetrical liver.

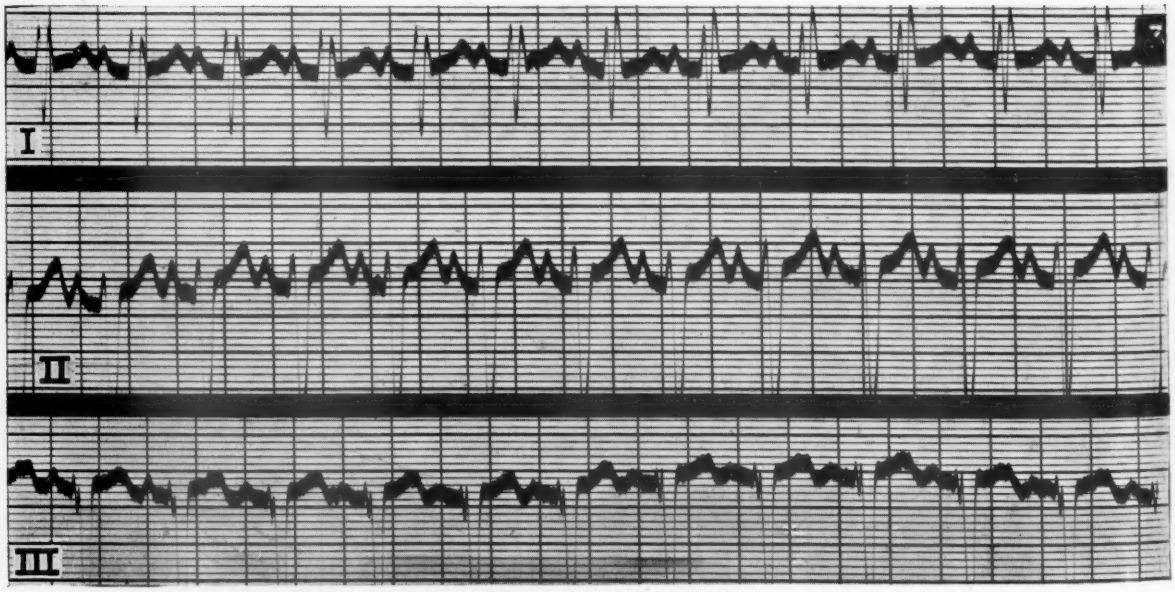

FIG. 2.—Case 1: electrocardiograph. (For description see text, p. 132.)

PLATE I

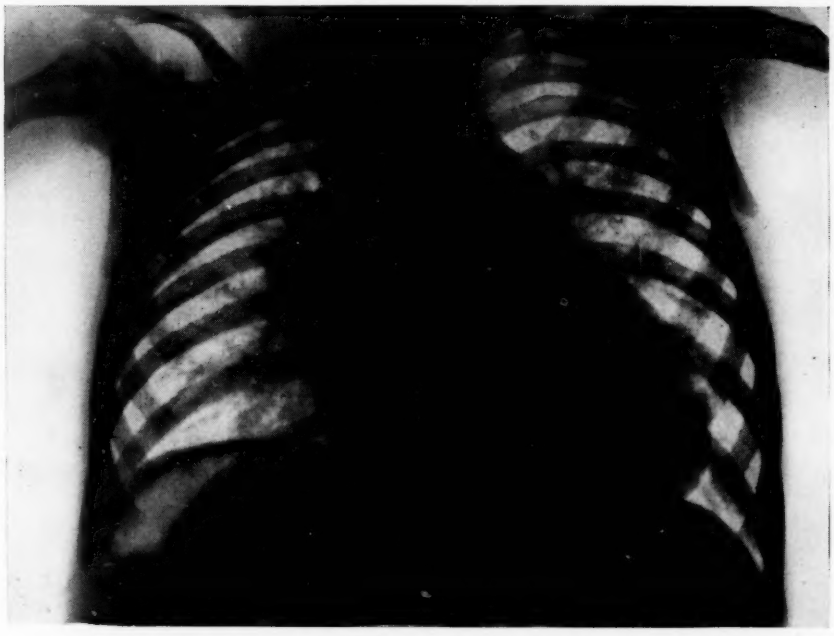

FIG. 3.—Case 2: radiograph showing heart in normal position with enlarged pulmonary conus, a stomach bubble under the right dome of the diaphragm, and post-pertussis hilar adenopathy on the right.

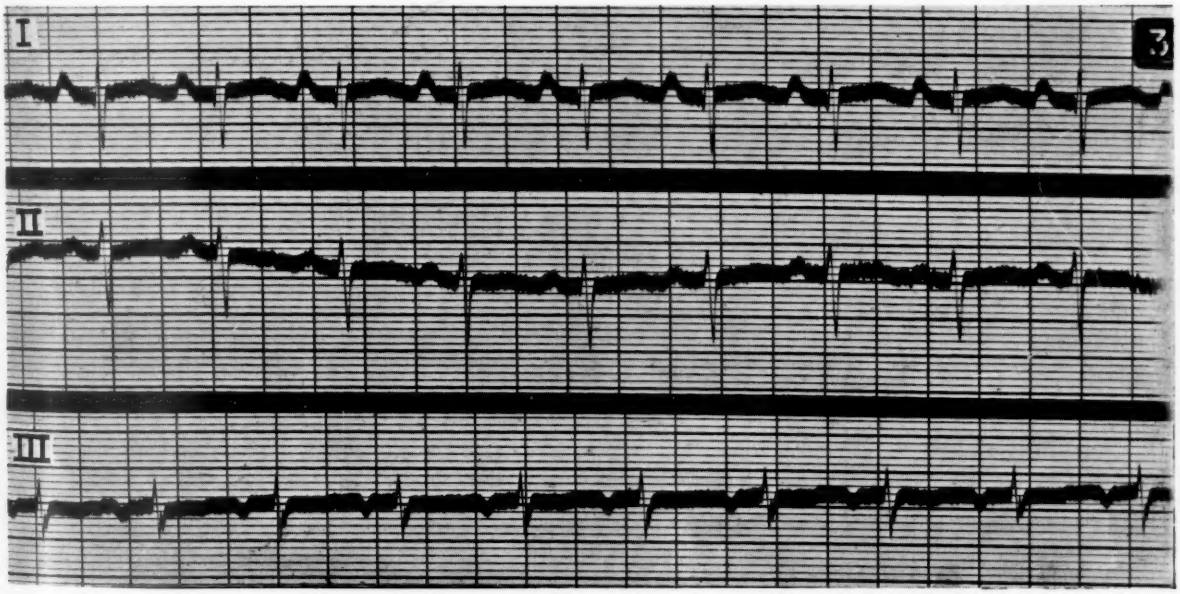

FIG. 4.—Case 2: electrocardiograph. (For description see text, p. 132.)

PLATE II

unnatural to expect that transposition of the vessels in some degree should be a feature, and defective septum is evidently associated with it. For the rest, it must be said that in all three autopsied cases there were numerous minor cardiac defects.

My grateful thanks are due to Dr. B. E. Schlesinger F.R.C.P., for his encouragement and permission to publish these cases. I would also like to thank Dr. D. J. Conway and Dr. P. V. Suckling for their assistance in preparing this article, and to the parents of the children for their co-operation.

Both cases were shown at a meeting of the Royal Society of Medicine in 1947.

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RADIAL NERVE PARALYSIS IN THE NEWBORN

BY

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(From the Mothers' Hospital, Clapton, London)

Wrist drop in the newborn caused by radial nerve paralysis is a rare phenomenon, although wrist drop due to intra-uterine position of the hand, that is, acute flexion at the wrist with pressure on the flexed hand, is not very uncommon. In a survey of the literature extending over a number of years comparatively few reported cases of wrist drop due to radial nerve paralysis occurring in the newborn were found. Two babies with neonatal radial nerve paralysis born within four weeks of one another have been seen recently at the Mothers' Hospital, Clapton, and are thought worth recording. A description is also given, for comparison with the other two, of a case of wrist drop due to intra-uterine pressure on the palmar flexed hand.

Case 1. Baby D had bilateral radial nerve paralysis due to antenatal trauma from a uterine contraction ring.

THE MOTHER. The mother was 40 years old, and had had one previous pregnancy in 1937, with normal labour.

She was admitted into hospital as an emergency because of prolonged labour. She had been in the first stage of labour for nine and a half hours, with strong frequent uterine contractions. Examination of the patient revealed a vertex presentation with no evidence of disproportion or of a pathological retraction ring (Bandl's ring). On vaginal examination the head was surrounded by an oedematous ring of cervix dilated to four fingers. In spite of good sedation and strong frequent uterine contractions every five minutes, with good relaxation between pains, labour progressed very slowly. After eight and a half hours the cervix was thought to be fully dilated, but under an anaesthetic a fine rim of cervix could be felt high up, through which the widest diameter of the head had already passed. An easy low forceps delivery was carried out under deep anaesthesia. There was some difficulty in delivering the shoulders. The cause of the delay in the first stage of labour was thought to be a contraction ring due to local tetanic uterine spasm. The reason for this diagnosis was the pressure marks on the infant, which are described below.

CONDITION OF INFANT AT BIRTH. The baby was born on Feb. 26, 1947, weighing 10 lb. 5¼ oz., and with white asphyxia; marked moulding of the head with caput, but no over-riding of the skull bones; cephalhaematoma of the right parietal region; bilateral wrist drop; evidence as described below of an antenatal ring of pressure encircling arms and trunk; and hypospadias (glandular). There was good recovery from white asphyxia.

The baby held its arms close to the side of the chest with the elbows acutely flexed, the forearms pronated, and the wrist, metacarpo-phalangeal, and interphalangeal joints flexed. On the lateral aspects of each arm just above the level of the elbow crease was an area of discoloured skin. The area of discoloration was roughly triangular in shape, the narrow apex of the triangle pointing forward, and measured about one and a half inches by three-quarters of an inch, that of the other arm being slightly the larger. Each area consisted of a central dark blue depressed, indurated patch with one or two pin-point areas of haemorrhage surrounded by a purplish bruised margin about one-half inch wide. With the arms at the side of the chest this band and the two pressure marks on the arms were at exactly the same level. The baby was unable to dorsiflex the wrists, supinate the forearms, or extend the fingers. The creases at the wrists, showing as a band of smooth pale pink skin, and the position (close to the chest) in which the arms were held suggested that antenatally the elbows had been acutely flexed and each hand had been tucked in a position of flexion into the axilla of the same side. There were no pressure marks on the forearms, hence the forearms must have been sufficiently extended at the elbow at the time the contraction ring developed to escape the direct pressure effect of the ring.

TREATMENT. The forearms were splinted with the wrists in dorsiflexion and the fingers were passively extended daily.

PROGRESS. Three days after delivery the constriction mark across the chest was no longer visible, although there was no noticeable improvement in the marks on the arms. Within a week from birth the baby was extending the forearms and waving the splints around. Extension of the fingers slowly improved, although there was as yet no active attempts at dorsiflexion of the wrists. By the eighth day the baby was able slightly to dorsiflex the wrists, the left a little more than the right. The amount of induration in the pressure areas on the arms increased, and reddish patches of pseudosclerema appeared in the skin and subcutaneous tissue of the neck and the back. The

bruised-like zone of pseudosclerema felt to the examiner not unlike the indurated areas in the arms. When the baby was discharged at 19 days old there was nearly full power of dorsiflexion at the wrists but full active extension of the fingers was not possible. At three months old, when seen again, the baby looked a healthy well-grown infant, the pseudosclerema had disappeared, and there was full range of movement in both upper limbs. There still remained in each arm a linear scar involving the skin and subcutaneous tissue, but the discoloration and induration had disappeared.

Case 2. Baby B had right radial nerve paralysis resulting from an obstetrical fracture of the humerus.

THE MOTHER. The mother was 24 years old, a primigravida. There was forceps delivery for primary uterine inertia continuing into the second stage.

CONDITION OF INFANT AT BIRTH. The child was born on March 22, 1947, and weighed 8 lb. 4 oz. The general condition was good, but there was simple transverse fracture of the humerus just above the middle of the shaft, with no obvious deformity. This was later confirmed by radiograph. All movements of the fingers and wrist joint, and the movements of flexion and extension of the elbow joint was present at birth. While the baby was undisturbed the upper arm lay flaccid by the side of the chest and there was no attempt on the part of the baby to move it.

TREATMENT. The upper arm was splinted with three straight splints, the elbow being flexed across the chest.

PROGRESS. A week later the characteristic posture of wrist drop had developed, with no active dorsiflexion of the wrists or extension of the metacarpo- and interphalangeal joints. The muscular tone of the forearm was diminished and there was some ulnar deviation. Owing to the age of the infant it was impossible to estimate the changes in skin sensitivity. There did not appear to have been any pressure in the axilla from the splints. A diagnosis of radial paralysis was made and the forearm was splinted with the wrist dorsiflexed.

Within three days the baby was able slightly to dorsiflex the wrist and extend the fingers. Full movement of the wrist and the fingers rapidly returned, and the forearm splint was removed seventeen days after delivery. The fracture of the humerus healed completely within one month from birth, and when discharged the infant had no evidence of radial paralysis and only a small amount of callus at the site of the fracture.

Case 3. Baby H had left wrist drop due to intra-uterine palmar flexion.

THE MOTHER. The mother was a primigravida 37 years old. She had forceps delivery for primary uterine inertia, continuing into the second stage.

CONDITION OF INFANT AT BIRTH. The baby was born on March 23, 1947, weighing 8 lb. 4 oz. The general condition was good. The left arm was held closely to the side of the chest with the elbow flexed. The forearm was pronated, the wrist palmar flexed, and the fingers clenched into the palm. The clenched hand fitted snugly into a depression below the left ear. There was a small area of red skin on the left arm near the insertion of the deltoid, but this was accounted for by the fact that the skin creased at this spot when the hand was held in the hollow below the left ear. The baby was unable to extend the hand at the wrist joint.

TREATMENT. A splint was applied to the left forearm with the hand slightly dorsiflexed.

PROGRESS. At one week old the baby could fully extend the fingers at all joints with the wrist flexed. The hand still assumed the position of wrist drop, but the wrist extensors were beginning to recover. When the infant was next seen at the out-patient clinic, shortly after discharge from the ward, there was full range of movement.

Discussion

The wrist drop in case 3 was clearly brought about by intra-uterine position, and intra-uterine position was considered as a possible cause of the wrist drop in case 1. However, in this case there was evidence of trauma of the soft tissues from pressure in an area where the radial nerve would be likely to be involved, and therefore it is reasonable to conclude that the trauma caused the paralysis.

Moreover, at least four other cases have been described closely resembling case 1, in each of which there was evidence of a band of pressure surrounding the trunk and arm and causing local trauma and radial nerve paralysis. The first was described by Brun in 1933 (quoted by Hauch and Ottsen, 1939). The baby had a dark, elongated transverse pressure mark on the outer side of the left arm, and on the same level a similar transverse pressure mark on the trunk. The mother was in labour four days, and the author attributed the baby's left radial nerve paralysis to the pressure of a " Bandl's ring " before birth.

It appears that the German authors apply the term " Bandl's ring " to the contraction ring, but in this country the name " Bandl's ring " is restricted to the retraction ring. The retraction ring (Bandl's ring of English textbooks) is a groove at the junction of the upper contracting and the lower passive uterine segments. It is present in every labour but does not normally rise above the symphysis. In obstructed labour, however, it becomes evident, running across the uterus. A contraction ring is a local spasm of the circular muscle of the uterus. It usually occurs in the lower uterine segment during the second stage of labour, but may occur anywhere in the uterus during any stage. The contraction

ring exerts great pressure and no progress occurs in the labour though pains continue.

Hauch and Ottsen in 1939 described another infant with left radial paralysis, also with a linear transverse pressure zone across the left arm and across the back on the same level. As in our case, there was deep infiltration of the tissue of the arm in the zone of pressure. The degree of trauma of the trunk was greater than in our case, and a biopsy, when the infant was one month old, of tissue from the zone of pressure showed inflammatory changes in the subcutaneous connective tissue and traumatic fatty necrosis. The authors consider that this may indicate the existence of previous "trophoneurotic" changes in the tissues predisposing to the pressure effect, which is interesting in view of the fact that pseudo-sclerema (localized subcutaneous fat necrosis) developed in our patient after birth. The mother had a long labour. Hauch and Ottsen considered there was no evidence to prove the existence of a "Bandl's ring" in this case, presumably using this term in the sense of a contraction ring, and attributed the long labour to a rigid cervix, but left undecided the origin of this transverse zone of pressure, as they were not able to suggest any other likely explanation.

Kehrer in 1918 gave an account of a new-born baby with bilateral radial nerve paralysis and pressure marks just below the middle of both upper arms. The marks on the outer side of each arm were thought to be due to pressure from the promontory and symphysis in a flat rachitic pelvis. It is not clear whether he considered the possibility of a uterine contraction ring, and one is tempted to suppose that these three cases may have been due, like ours, to such a ring of constriction.

A fourth case of bilateral radial nerve paralysis found by Hauch and Ottsen in their hospital records was born to a mother with a long labour and again a 'Bandl's ring.' Hauch and Ottsen in 1939 were able to find twenty-five cases of neonatal radial nerve paralysis in the literature, found six more in their hospital records, and added two more cases of their own, making thirty-two in all. All these were apparently due to trauma of the peripheral part of the radial nerve. It is surprising that only two of these were due to involvement of the nerve at the site of a fracture and it seems probable that this etiology is more common than the figures would suggest.

The prognosis of neonatal radial nerve paralysis is good.

Summary

Two cases of radial nerve paralysis in the newborn are presented, one due to pressure from a uterine contraction ring, the other due to involvement of the radial nerve at the site of a fracture.

I wish to thank Dr. H. M. M. Mackay for her permission to publish these cases, and for her encouragement and helpful advice.

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BRITISH PAEDIATRIC ASSOCIATION

PROCEEDINGS OF THE NINETEENTH GENERAL MEETING

The Nineteenth Annual Meeting of the British Paediatric Association was held at Windermere on April 16 and 17, 1948.

Business proceedings; The President, Dr. Donald Paterson, was in the Chair, and the following members were present:

Drs. F. M. B. Allen, H. T. Ashby, C. Asher, J. M. Bligh, F. Braid, J. V. Braithwaite, R. W. Brookfield, D. J. W. Browne, H. C. Cameron, C. Chisholm, W. H. P. Cant, N. B. Capon, W. R. F. Collis, T. Colver, B. D. Corner, J. Craig, W. S. Craig, J. Crooks, G. Davison, R. H. Dobbs, E. Dott, R. W. B. Ellis, P. R. Evans, G. B. Fleming, F. J. Ford, A. W. Franklin, W. F. Gaisford, S. Graham, H. H. C. Gregory, C. K. J. Hamilton, C. F. Harris, J. D. Hay, H. Helmholz, J. L. Henderson, D. V. Hubble, N. M. Jacoby, H. E. Jones, R. Lightwood, A. MacGregor, H. M. M. Mackay, A. G. Maitland-Jones, R. Marshall, C. McNeil, F. J. W. Miller, A. Moncrieff, A. E. Naish, A. V. Neale, G. H. Newns, D. N. Nicholson, A. G. Ogilvie, J. N. O'Reilly, C. G. Parsons, L. Parsons, D. Paterson, W. W. Payne, C. B. Perry, C. P. Pinckney, C. T. Potter, B. Schlesinger, W. P. H. Sheldon, W. C. Smallwood, J. M. Smellie, R. E. Smith, J. C. Spence, R. E. Steen, H. H. Stewart, K. H. Tallerman, M. L. Thomson, C. W. Vining, H. L. Wallace, H. K. Waller, J. F. Ward, A. G. Watkins, T. P. Williams, M. J. Wilmers, D. W. Winnicott, W. G. Wyllie.

There were also fifty-seven guests including Dr. B. Landtman of Helsinki.

The MINUTES of the last Annual General Meeting were approved.

ELECTION OF OFFICERS: The following were unanimously elected by ballot for the year 1948-49:

PRESIDENT: Dr. H. T. Ashby, Manchester.
TREASURER: Dr. R. C. Lightwood, London.
SECRETARY: Prof. Alan Moncrieff, London.

EXECUTIVE COMMITTEE (to replace those retiring):

REPRESENTATIVE FOR PROVINCES: Dr. G. Davison, Northumberland.
REPRESENTATIVE FOR SCOTLAND: Dr. J. H. Hutchison, Glasgow.

ELECTION OF NEW MEMBERS: The following were elected by ballot to membership of the Association:

(a) HONORARY MEMBERS:
Dr. H. H. Chodak Gregory, Huntingdon.
Dr. E. W. N. Hobhouse, London.
Prof. R. A. McCance, F.R.S., Cambridge.
Dr. D. Paterson, Canada.

(b) CORRESPONDING MEMBERS:
Prof. G. Fanconi (Zurich).
Prof. A. Lichtenstein (Stockholm).

(c) ORDINARY MEMBERS:
Dr. E. C. Allibone, Leeds.
Dr. H. S. Baar, Birmingham.
Dr. R. E. Bonham Carter, London.
Dr. I. A. B. Cathie, London.
Dr. Mary Crosse, Birmingham.
Dr. D. Gairdner, Cambridge.
Dr. E. W. Hart, London.

THE TREASURER'S REPORT was received and approved. It was agreed to give financial support to the proposed International Pediatric Association on the suggested basis of 75 cents per member per annum.

THE SECRETARY'S REPORT was received and approved and is printed below.

NEXT PLACE OF MEETING: This was left to the Executive Committee.

ALTERATION OF RULES: Rule 3: It was agreed that for 'six ordinary members' this should now read 'eight ordinary members' (members of Executive Committee).

Rule 12: It was agreed that for 'one month' this should now read 'two months' (notice for the proposal of new members). The consequential alterations in rules 4 and 18 were also approved.

Secretary's Report on Activities of Executive Committee

(1947-48)

Mr. President, Ladies and Gentlemen,

Since the last Annual General Meeting held in Windermere in April, 1947, the Executive Committee has met on four occasions. The following is a brief summary of the main activities during the year.

1. APPOINTMENTS AND DISTINCTIONS: The Association will wish to join with the Executive Committee in congratulating Sir Leonard Parsons on his election as F.R.S., a distinction for paediatrics and a fitting tribute to his life-long work and interest. Congratulations were also sent during the year to the following members elected to new University chairs: W. F. Gaisford (Manchester), A. V. Neale (Bristol), and J. Craig (Aberdeen).

2. OBITUARIES: The Association has suffered considerable loss during the year in the deaths of

the following: Corresponding Members—H. B. Cushing (Montreal), C. Louis Leipoldt (Capetown); Honorary Members—Leonard Findlay, Noah Morris, Sir John Fraser; Ordinary Member—C. Paget Lapage.

3. MEMBERSHIP AND FUTURE POLICY: The Executive Committee, after discussing this matter in some detail, circulated a questionnaire to all members. As already stated in a circular letter, no clear mandate was received for any radical change in constitution. It was therefore decided not to prepare any new rules for the 1948 annual meeting but to foster the development of regional paediatric groups and after a suitable interval to review such organizations in the light of their implications for changes in the constitution of the central body.

4. INTERNATIONAL MEETINGS: At the Fifth International Pediatric Congress in New York in July there were fifteen members of the Association present as well as fourteen others from the British Isles. It has been decided to frame a constitution for an International Pediatric Association, and your secretary has been asked to serve on a committee for this purpose. Ratification of any proposals will take place at the next International Congress in Zurich in August, 1950, and meanwhile the Association has been asked its views on financial support for the international organization. The section on paediatrics of the International Conference of Physicians held in London in September, 1947, was well attended.

5. HOSPITALS AND PLANNING: Formed at the instigation of the Association, a paediatric planning committee for the North-west Metropolitan Region has continued its activities during the year and a final report is being prepared. The Association has been asked for help in regard to various hospital and local authority appointments and the secretary has corresponded with most of the bodies whose advertisements have appeared during the year, sending copies of the circular on the appointment of a consulting paediatrician. Sub-committees have visited Cheltenham and Blackburn and reports to the authorities in these areas have been approved by the Executive Committee.

6. CHILD GUIDANCE: During the year the Executive Committee and its child psychology sub-committee has devoted considerable time to this subject. It has agreed to press for the development of psychiatric departments in all children's hospitals, to seek closer liaison with the child guidance group of the National Association for Mental Health and to impress upon the Ministry of Education and local Education Authorities the importance of securing that a psychiatrist trained in children's work and a paediatrician take part in all child guidance activities.

7. SUB-COMMITTEES AND REPRESENTATIVES ON OTHER BODIES: In addition to the work mentioned in the last paragraph, sub-committees which have been active during the year include the following: Nursing Committee (jointly with the Association of Sick Children's Hospital Nurses): a memorandum has been circulated concerning the Working Party's Report on Nursing.

Hospital Architecture and Cross Infection: statistical analysis of the returns on cross infection is now proceeding, the Ministry of Health having made a grant for this purpose.

Post-war Convalescent Homes (jointly with the I.C.A.A. and Institute of Almoners): policy with regard to provision of machinery for convalescence has been elaborated.

The report of the sub-committee on Neonatal Mortality (jointly with the Royal College of Obstetricians and Gynaecologists) is to be published by the Ministry of Health. It has been decided to dissolve this committee now that the report is finished and also the rheumatism committee and the committee on hospital undergraduate teaching.

Dr. C. F. Harris has been co-opted to the Public Health Committee of the British Medical Association. The secretary has been appointed to a committee of the Royal College of Obstetricians and Gynaecologists on maternity hospital reports and Mr. Denis Browne to a committee of the British Standards Institute on Surgical Instruments.

8. WINDERMERE LECTURESHIP: The Executive Committee has accepted from Messrs. Cow and Gate Ltd. a generous gift to provide funds for a biennial lectureship by a distinguished paediatrician from abroad and the Association is fortunate in being able to welcome Dr. Henry Helmholz, who was the President of the International Congress in New York, as the first lecturer.

9. VISIT TO SWEDEN: At the kind invitation of the Section on Pediatrics and School Hygiene of the Swedish Medical Society a party of members numbering about thirty will visit Sweden at the end of May.

10. MILK: The Executive Committee has discussed the supply of evaporated milk to hospitals and there has been correspondence with the Ministry of Food on this subject. The secretary will supply details to any member who requires information. The Committee was also asked by the Ministry of Health for views on the addition of iron to dried milk and there was a large majority against this as a routine measure.

11. CARE OF THE MENTALLY DEFECTIVE CHILD. At the suggestion of Professor Vining a resolution has been sent to the Ministry of Health for circulation to the regional hospital boards stressing the urgent need for greater provision of institutional care for children who are mentally defective.

12. ACTING-CHAIRMAN OF EXECUTIVE COMMITTEE: It was decided to record the deep gratitude felt by the Committee to Professor Vining for acting as Chairman during the year 1947-48, an additional year after his official term of office had ended.

ALAN MONCRIEFF.

Communications

1. DR. A. P. NORMAN (London) (introduced by Dr. C. F. Harris): 'Spina Bifida Cystica.' Survey of the literature on meningoceles gives little information on the advisability of, and the indications for, operation; nor on the development of hydrocephalus. Analysis of 161 cases of spina bifida cystica seen at the Hospital for Sick Children, Great Ormond Street, London, showed that more than a third were alive, more than a third dead, and the majority of the remainder probably dead. The operative mortality was twice as great in the first month of life as afterwards, and it is known that the operative mortality is very small after the age of two. Early operation would therefore be indicated only if rupture of the sac were a common cause of early death, and this it was not possible to show.

Eleven children out of sixty who had no paralysis before operation developed a neurological lesion other than hydrocephalus after operation; this does not include fatal cases.

Established hydrocephalus did not seem to be made worse by operation, but the likelihood of death after operation was much greater than in the uncomplicated case. Seven children appeared to develop hydrocephalus after operation, but it is not certain that their heads had regularly been measured beforehand. Hydrocephalus was first noted mostly in the first months of life but the incidence throughout the first year was similar in pre- and post-operative cases.

It is suggested that there is no evidence to show that operation is beneficial; if performed, it should be on uncomplicated cases after the age of one year. More basic facts would be obtained if each paediatric centre could adopt a standard scheme of investigation and treatment.

2. DR. C. BALF (Edinburgh) (introduced by Dr. H. L. Wallace): 'Neonatal Behaviour of Infants Born (a) by Spontaneous and (b) by Forceps Delivery.' A preliminary investigation has been made of the behaviour of babies born by spontaneous and forceps delivery to determine what neonatal abnormalities may be related to subsequent mental or physical defect. Clinical examination was restricted to those weighing between 5½ and 10 lb. at birth.

The Moro response was found to vary with other clinical measures of cerebral changes, but, in addition, numerous minor variations in the response were found more frequently after abnormal delivery. Systematic clinical examination in the first two days showed minimal evidence of cerebral disorders in 5·9 per cent. of spontaneous deliveries (mostly primiparous mothers), and in 23 per cent. of forceps deliveries. These figures corresponded well with the difficulty of labour judged from the obstetric reports and the evidence of foetal distress. Persistent vomiting was noted in 20 per cent. of the abnormal deliveries, but only in 1 per cent. of the normal. There was often no other evidence of cerebral irritation, though such babies fed slowly and were late in fixing to the breast.

Day-to-day variations in body temperatures were greater after instrumental delivery, and a characteristic saw-toothed temperature chart was often seen. Fever on the second to third day associated with clinical dehydration occurred far more frequently after forceps delivery despite the special attention given to the fluid intake for such babies. There was no direct correlation between irregularities of temperature and persistent vomiting, but they are judged symptomatic of some cerebral dysfunction.

3. DR. G. MONTGOMERY (Glasgow) (introduced by Professor S. Graham): 'The Pathological Findings in Eight Fatal Cases of Tuberculous Meningitis Treated with Streptomycin.' The findings were described in eight fatal cases of tuberculous meningitis treated by streptomycin in the Royal Hospital for Sick Children, Glasgow, demonstrating progressive meningeal tubercles associated with regressive lesions in other organs.

Meningeal lesions. All the cases had soft gelatinous exudate and groups of fresh tubercle follicles similar to those usually found in untreated cases of tuberculous meningitis. Tubercle bacilli were cultured from the cerebrospinal fluid after death and showed no increased sensitivity to streptomycin. In three cases there were cortical tuberculomata, and in all the cases the cerebral sulci contained tubercle follicles which had clearly been proliferating at the time of death.

Lung lesions. Five of the eight cases had caseous primary foci which showed degrees of encapsulation no greater than in untreated cases; in one no primary focus was found but there was a small calcified hilum gland; and in two cases the focus was represented by scar tissue with hyalinized follicles.

Miliary tubercles. These showed varying degrees of hyaline degeneration, the epithelioid cells had disappeared, and tubercle bacilli could not be demonstrated. Hyaline degeneration occurs in tuberculous lesions which heal spontaneously by fibrosis, but the feature of the streptomycin cases is the complete hyalinization of follicles which show no evidence of antecedent fibrosis and thus offer morphological evidence of the chemotherapeutic effect.

4. DR. C. ASHER (London): 'The Relation of Birth Weight to Mental Development.' The literature is conflicting. There are two main methods of approach to the problem: (1) the follow-up method (this has the disadvantage that a large number of children remain untraced); (2) the indirect method of ascertaining what proportion of individuals of known intellectual levels were immaturely born. This was the method used in the study here reported, in which 5,177 school-children were investigated. It was found that there was a significantly higher proportion of immaturely born children in the special schools for educationally

subnormal than in all the other schools (grammar, modern, and primary). Also the mean birth weights of the educationally subnormal pupils were significantly lower than the mean birth weights of the pupils in all the other schools. The fact was therefore established that there was some connexion between low birth weight and mental development. It was difficult, however, to decide whether the immaturity was the cause or the effect of the educational subnormality. Birth trauma or anoxaemia in an immaturely born infant might be responsible for failure in mental development, or the child might be born immaturely because of some innate mental or physical defect. Moreover the genetic factor had to be considered.

It was thought that a nutritional factor was probably not involved, as all the children were drawn from the same area. The work was carried out on Finchley (Middlesex) schoolchildren.

5. Dr. T. Wright (Sheffield) (introduced by Professor R. S. Illingworth): 'The Incidence and Possible Significance of the Choroidal Tubercle.' There have been twenty papers on the subject in the Index Medicus during the past nineteen years. The literature is confused as regards the incidence of the tubercles, an average of 14·6 per cent. in tuberculous meningitis and 50 per cent. in miliary tuberculosis with meningitis being reported.

In a series of fifty consecutive cases our figures are as shown:

	Number of cases	Number of cases with choroidal tubercles	Per cent.
Meningitis + Miliary ..	26	16	61·5
Meningitis ..	15	1	6·6
Miliary ..	9	3	33·3
Total ..	50	20	

The choroidal tubercle is not a terminal phenomenon. The natural history of the choroidal tubercle is one of enlargement and hardening of outline, a gradual change in colour from yellow to parchment white, and the formation of a surrounding zone of black pigment. These changes are not attributable to streptomycin therapy.

Although by no means a complete guide, the changes in the choroidal tubercle may be of help in assessing the prognosis of the case. Choroidal tubercles have not been observed to disappear when the underlying tuberculous process is healing or has healed. Choroidal tubercles have been observed only very rarely in tuberculous meningitis, and this is suggestive that there is an associated miliary tuberculosis. Choroidal tubercles have been observed in two cases without obvious miliary tuberculosis. No streptomycin therapy was given. The patients are well and the choroidal tubercles are in the late stage, which we suggest implies that they are healed.

6. Professor J. C. Spence (Newcastle): 'The Initial Illness of Poliomyelitis.' Newcastle had a brisk experience of poliomyelitis in the recent epidemic, when 184 cases were studied in the Children's Department and associated hospitals. The epidemic followed the normal modern course, with rising age incidence and a correlated increased mortality in the older patients. Particular attention was directed to the initial illness and its relationship to the neck stiffness or paralytic illness which may follow it. The speaker stressed the importance of studying the initial illness by saying that it is doubtful if we shall make any real advance in understanding the epidemiology of poliomyelitis until we find means of diagnosing the initial illness, and that mere elaboration of the diagnostic signs of paralysis will teach us little. The initial illness is best studied when there is a distinct interval of recovery before the onset of neck stiffness or paralysis. It usually lasts about thirty-six hours but may be as brief as six. It was present in seventy-six of the 184 cases studied. Although the illness is difficult to diagnose in our present stage of knowledge some clinical features were very suggestive, particularly the combination of a peculiar physical lethargy with mental clarity in a febrile child, the illness starting abruptly and often ending abruptly. The interval between the initial illness and paralytic illness was variable, anything from one to nineteen days in the speaker's experience. There was evidence that heavy muscular exercise with exhaustion in the interval following the initial illness might precipitate a paralytic illness, and cases were quoted in support of this view.

A plea was made for a clarification of our terms in this disease, avoiding such phrases as 'abortive poliomyelitis' and 'pre-paralytic poliomyelitis.' Professor Spence suggested that the stages of disease should be clearly designated: (1) the initial illness; (2) the interval period of apparent recovery; (3) the main illness involving invasion of the child's nervous system; and (4) the stage of permanent paralysis.

7. Dr. B. Schlesinger (London): 'The Treatment of Liver Failure in Gastro-enteritis with Casein Hydrolysate.' The clinical picture of this fatal complication of gastro-enteritis is characterized by sudden rapid deterioration of the infant, increased dehydration despite the usual measures, a haemorrhagic diathesis manifested by purpura or melaena and haematamesis, and rapid enlargement of the liver. Sometimes the true nature of the condition remains unsuspected until the advent of jaundice. Urgent treatment is necessary, and every effort should be made to recognize the condition at an early stage.

As a result of animal experiments and reports on children in the tropics or in occupied countries in

Europe who had had diets grossly deficient in protein, the lesion suspected was disorganization of the liver cells, often with fatty infiltration progressing eventually to fibrosis. This was brought about by the continued deprivation of protein together with other dietetic components through long-standing gastro-enteritis.

To combat this, and to supply the necessary lipotropic agent, casein hydrolysate was administered. It had the advantage of being easily assimilable and of providing readily available methionine and an adequate calorie intake to tide the infant over its most critical period. The oral route was preferable as it was difficult to obtain a sufficient amount quickly if given intravenously in a strength and at a rate suitable for the size of the infant. Moreover, it was notoriously difficult to keep solutions of amino acids sterile when using this method. Nevertheless with intractable vomiting the intravenous route was successfully employed. The speaker found that 70 g. of casein hydrolysate containing 50 per cent. of protein and 50 per cent. of lactose was usually well tolerated by infants weighing 12 to 13 lb. Ten grammes were dissolved in 5 or 6 oz. of water and given repeatedly in seven feeds. In addition choline was administered orally (0·1 to 0·2 g. daily) as a supplement to spare the methionine present in the casein hydrolysate. The treatment was continued in face of diarrhoea, which eventually subsided spontaneously, until the signs of liver failure abated. Breast milk was gradually added to the diet as the digestion became more tolerant.

Ancillary treatment was used, such as the maintenance of hydration, the correction of an upset acid-base balance, and the provision of the necessary vitamins. When purpura was present, vitamin K was added. Sulphadiazine was employed in the presence of some parenteral infection.

None of these routine measures was successful in overcoming the complication of liver failure in the past. With the use of casein hydrolysate in seven cases, the last four by the oral route alone, all had recovered from a condition which was rapidly advancing in the same fatal direction.

8. Dr. F. R. M. Elgood (Cardiff) (introduced by Dr. A. G. Watkins): 'Intestinal Distension in Infants.' There is a type of intestinal distension that occurs at the end of prolonged illness in infancy, associated with hepatic enlargement, cachectic purpura, and haematemesis. It is found in gastro-enteritis resistant to treatment, after prolonged partial starvation and intravenous therapy. At necropsy an enlarged fatty liver and distended intestines with superficial erosions are found.

Rutin, vitamin K, adrenal cortical extract, and fresh blood proved valueless in this condition. Choline chloride is effective in preventing fatty degeneration of the liver in doses of 0·25 to 0·5 g. three times a day by mouth. Carbohydrate and protein also protect the liver, and were given intravenously as 600 to 1,000 ml. per day of equal parts of 5 per cent. glucose and plasma. Improved results were obtained if full-strength half cream one-ounce milk feeds were given four-hourly.

Vitamin B_1 deficiency occurs rapidly in starvation. Vitamin B_1 has also a stimulant effect on the bowel. Six-hourly injection of 2 mg. of vitamin B_1 causes a rapid subsidence of the distension. Before this treatment all our cases developing this condition died. Since we decided to institute it at the first sign of liver enlargement, two cases have died, of other causes after having been apparently cured, one died soon after treatment was begun, and three have recovered. The numbers are small, as the condition is rare, but I have been impressed with the results so far obtained.

9. Dr. White Franklin (London) 'The Place of the Residential School in the Treatment of Bronchiectatic Children.' The Invalid Children's Aid Association, inspired by Dr. Elaine Field, two and a half years ago opened the Meath Hospital School at Ottershaw, Surrey, with twenty-four beds for boys aged two to seven and girls aged two to ten years. The daily routine includes two periods of an hour's physiotherapy and two periods of two hours' schooling. Postural drainage on tip beds is used in suitable cases. Seventy-three children have been treated, the longest for two years, the shortest for three weeks, the records of sixty-five forming the basis for the report. Of these, twenty-seven were severe cases, nine moderately severe, and twenty-nine mild with little clinical evidence of disease. There were sixteen surgical cases, mainly severe.

The mild cases have made the greatest improvement, when judged by general betterment and amount of cough, sputum, and nasal discharge. Poor posture and chest expansion responded well to physiotherapy. Changes in weight were difficult to assess, as low weight and failure to gain are not found except in the most severe or in complicated cases. Penicillin inhalations (sixteen cases) did not help the severe but did benefit the mild cases. Surgical treatment did not seem to have accomplished much in this particular series. A follow-up study of twenty-nine children brought out the importance of bad home conditions in relapses. On the other hand long separation from home in the early years of life had occurred in the four boys most difficult to control. Thirty-one cases, including the most severe, had started coughing under the age of one year and forty-seven under two, so that prevention demands special care in infancy. While no dramatic improvement was noted in the series, the home was able to provide continuous schooling and physiotherapy under good conditions for the severe cases, with a chance of drying up for the mild ones.

10. Dr. C. J. Hodson and Dr. C. A. Neill (London) (introduced by Dr. H. M. Mackay):

'Post-pneumonic Pneumatocele.' The air-containing lesions associated with pulmonary consolidation in children have been well described in America. Views over there, however, differ as to their late results. Some authors (Caffey, 1940) state that they clear up completely leaving no trace even after having persisted for months, others (Pierce and Dirkse) that they may be the cause of 'congenital' cystic disease and bronchiectasis.

In the present communication six cases were described and illustrated. The oldest was fifteen months. They showed air-containing spaces occurring with a variety of pulmonary lesions including staphylococcal pneumonia, lobar pneumonia, a possible original fluid-containing congenital cyst, localized pneumonic consolidation, and one case showing consolidation-collapse without pyrexia. Two cases were complicated by pneumothorax. One, a doubtful case, recurred seven years later and was excised, another showed a neonatal bilateral pneumothorax. Most of the cysts and their complications cleared rapidly leaving no apparent trace. One still remained after five months, but was getting smaller. A mixed bacteriology including staphylococci, haemolytic streptococci and pneumococci was obtained, and all febrile cases had received chemotherapy.

It was suggested that there was a scarcity of post-mortem and other evidence as to whether all 'pneumatoceles' were of a similar etiology or whether they arose from a variety of conditions. Doubt was expressed as to whether they did all in fact resolve completely, and a plea was made for (1) early radiography of every case of pulmonary infection in the very young to ascertain their etiology; (2) a prolonged follow-up of cases with bronchography to assess their late effects.

Caffey, J. (1940). *Amer. J. Dis. Child.*, **60**, 586.
Pierce, C. B., and Dirkse, P. R. (1937). *Radiology*, **28**, 651.

11. DR. M. E. MACGREGOR (London) (introduced by Dr. R. C. Lightwood): 'Some Observations concerning Renal Calcification in Infancy.' The clinical histories were analysed of twenty-five children, all less than two years old, who showed calcification in the medulla of the kidneys at necropsy. Any feature shared by them all which might cast light upon the pathogenesis of their lesion, or assist in their diagnosis during life, was sought for. Further, the numbers that fulfilled the conditions of a syndrome described by Lightwood in May, 1935, were determined. No factor other than loss of weight was found to be applicable to the entire group, but eighteen cases were able to be classified as belonging to the group described by Lightwood. All but one of the remaining seven cases showed gross associated pathology, sufficient by itself to cause death.

A series of 230 kidneys derived from routine post-mortem material from children under two years of age was then examined histologically. Cases that had died of primary renal disease were excluded. In twenty-four instances (11 per cent.) renal calcification was present, in seventeen of which it was present in the medulla. The clinical records of these seventeen cases revealed that six conformed to Lightwood's description; eleven did not. Among the latter group, who died from very diverse conditions, no common link could be established. It was concluded that, although twenty-four out of forty-four examples of medullary calcification belonged clinically to the group described by Lightwood in 1935, precisely similar calcification was to be encountered in this age group in many other conditions which were apparently quite unrelated to each other.

12. DR. W. W. PAYNE (London): 'Persistent Acidosis in Infancy.' A case of nephrocalcinosis of the Albright type was found in a child and an attempt was made to see if the type of nephrocalcinosis described by Lightwood could be a forerunner of that condition. The history of the case of Albright syndrome was that the child was normal for the first eighteen months of life and was then admitted to another hospital with 'kidney trouble.' Owing to evacuation, no further history is available until she was seen at the Hospital for Sick Children, London, where the provisional diagnosis of renal rickets was made. There was profound decalcification of the bones, muscular weakness, thirst (but normal appetite), and albumin, blood, and pus in the urine.

The cases of the Lightwood syndrome were all under one year and had illness of over four weeks, consisting of anorexia (which was often very marked), constipation, loss of weight, vomiting, hypotonia, and dehydration. The urine contained leucocytes, epithelial cells, and often a trace of albumin, and was constantly sterile and often alkaline. An additional symptom present in about half the cases was thirst.

There was thus no great resemblance between the two syndromes clinically. Chemically, however, there were certain points of resemblance. The Albright type showed acidosis with persistently raised blood chlorides as well as the changes in the calcium and phosphorus to be expected from the bony condition. Seven cases of the Lightwood syndrome all showed persistent acidosis and similarly raised chlorides with no alteration of the calcium and phosphorus. The raised chlorides were greater than would be caused by the degree of acidosis. The presence of an alkaline urine with persistent acidosis is a point of diagnostic value. All the cases were treated with the citric acid-sodium citrate mixture of Albright and showed very considerable clinical improvement. Some cases required very large doses, amounting to between 9 and 15 g. of sodium citrate daily, before the acidosis was corrected.

Taking into consideration the results of MacGregor, it was concluded that there was no conclusive evidence that the nephrocalcinosis of the post-mortem room and the nephrocalcinosis of the

Albright type were identical with the Lightwood syndrome. It was suggested that the group of cases described by Lightwood should be called Lightwood's syndrome, as 'persistent acidosis' is too general a term.

Albright, F., Consolazio, W. V., Coombs, F. S., Sulkowitch, H. W., and Tabbott, J. H. (1940). *Bull. Johns Hopk. Hosp.*, **66**, 7.

13. DR. J. D. PICKUP (Leeds) (introduced by Professor W. S. Craig): 'Some Clinical Aspects of Oesophageal Obstruction in Children.' In two years eight cases of oesophageal stenosis were seen, seven of which were boys and two of which were premature. Five cases had a history of vomiting from birth, and all became worse when thickened feeds were introduced into the diet. The typical clinical features are that the child is extremely hungry and often grossly underweight. The older child takes the food deliberately, pausing until the food has passed through the stricture, and during the pause he may make characteristic forced swallowing movements, craning the neck forward, opening the mouth, and contracting and relaxing the pharyngeal and buccal muscles. In five cases blood was found in the vomit.

A tendency to severe exacerbations in which both solids and liquids were returned, was seen in five cases; these became so obstructed that dilatation by bougies had to be resorted to, and two required gastrostomy. The milder cases do reasonably well on a semi-solid diet, but all remain greatly underweight and often stunted in height.

A case showing a 'corkscrew' deformity of the lower third of the oesophagus was described. Another boy with a short oesophagus and large hiatus hernia had no symptoms referable to the gastro-intestinal tract but had a red cell count of 730,000 per c.mm. and a haemoglobin of 14 per cent., this was thought to be due to a constriction of the cardiac end of the stomach with continual oozing of blood, a condition previously described by Murphy as 'hiatus hernia anaemia.'

14. DR. K. H. TALLERMAN (London): 'Some Comments on the Present Incidence of the Rheumatic Infection in Childhood.' The memorandum produced by the British Paediatric Association on this subject a few years ago indicated that the incidence of this disease had decreased between 1937 and 1942. On returning to civil practice after an absence from paediatrics of three and a half years the speaker was forcibly struck by the infrequency with which cases suffering from acute and sub-acute rheumatism, chorea, and rheumatic carditis were appearing in the children's department of the London Hospital, which confirmed his views that this disease was less prevalent than of old, and he thought it worth while analysing the two-year period from June, 1945, to May, 1947, and comparing it with a similar two-year period, 1937 to 1939.

From his figures it was apparent that the percentage of rheumatic cases to total admissions or out patient attendances had fallen by half in the latter as compared with the earlier period (see table).

A decrease had also been observed in the number of children coming as out patients on account of mild chorea, which had dropped from twenty-three in the earlier period to one in the later.

All the evidence appeared to indicate that the rheumatic infection was less prevalent now than of old, and the decrease in incidence reported as occurring until 1942 was still noticeable up to the spring of 1947. An increase in incidence occurred during the winter of 1947 to 1948, but the speaker regarded that as probably only a temporary phenomenon in view of the consistent fall over a period of years.

RHEUMATIC FEVER IN CHILDHOOD (DR. K. H. TALLERMAN)

TABLE

Period	Number of children under 14 years dealt with at the London Hospital		Number of rheumatic children under 14 years dealt with at the London Hospital		Per cent. of rheumatic to total admissions	Per cent. of rheumatic to total new out patient cases
	Admitted to hospital	New cases attending as out patients	Admitted to hospital	New cases attending as out patients		
June, 1937, to May, 1939 ..	1,431	2,836	129	66	9	2·3
June, 1945, to May, 1947 ..	743	1,886	30	14	4	1·4

* The actual number of children on the school attendance roll of the London County Council in the area served by the hospital in July, 1939, was 104,932; in July, 1946, it was 52,533, a decrease of 52,399.

REVIEWS

Garrod, Batten and Thursfield's Diseases of Children. Fourth Edition. Edited by DONALD PATERSON, M.D. (Edin.), F.R.C.P., Physician, Hospital for Sick Children, Great Ormond Street; Physician in charge of Diseases of Children, Westminster Hospital; and ALAN MONCRIEFF, M.D. (Lond.), F.R.C.P., Nuffield Professor of Child Health, University of London; Physician to Out-patients, Hospital for Sick Children, Great Ormond Street; Physician, Children's Department, Middlesex Hospital. Vol. I, with contributions by twenty-nine contributors. 1947. London: Edward Arnold and Co. Pp. 771. (Price 30*s.*)

The death of Dr. Hugh Thursfield since the third edition was published in 1934 has removed the last of the original editors of this standard work, and one who was also one of the two original editors of the Archives of Disease in Childhood. The connexion with this journal, however, is still a close one, since Dr. Paterson is a member of the editorial committee, and Professor Moncrieff a former editor. With the Hospital for Sick Children, Great Ormond Street, London, the connexion is even closer, and though a number of other schools are represented, including the Harvard Medical School and the University of Pennsylvania, the volume will continue to be identified to a large extent with the teaching and practice of that hospital. The present edition has been divided into two volumes, and contains many new features, amongst which the sections on vital statistics and administration (Dr. J. A. Charles), growth and development (the late Professor N. Morris), and water and electrolyte control (Professor McN. Scott) are indicative of the various lines along which the science of paediatrics has advanced during recent years. These are included in Part I (General Considerations), whilst Part II deals more specifically with diseases of children, including the neonatal period, tuberculosis, allergy, and diseases of nutrition, metabolism, the ductless glands, the alimentary system, and the upper and lower respiratory tract. Dr. Paterson contributes a section on infant feeding, and Professor N. B. Capon's section on the newborn calls for special mention as an admirable presentation.

Since such a wide variety of paediatric interests are represented (medical, surgical, dental, biochemical, pathological, genetic, and statistical), it is inevitable that there is some inequality of style and emphasis. But the editorial whip has evidently been cracked to such good effect that a winning team (however oddly assorted in age and pace) has successfully been driven home, dragging behind it triumphantly the first half of the friendly and familiar Great Ormond Street Omnibus. We feel every confidence that the book will long retain its well-deserved popularity.

Polycories. By ROBERT DEBRÉ. 1948. Paris: C. Doin et Cie. Pp. 126. (Price 215 *fr.*)

In this useful monograph, Professor Debré reviews the various clinical, biochemical, and pathological features of glycogen disease, the hepatomegaly occasionally seen in juvenile diabetics, and the type of lipoid storage described by the author and Dr. Semelaigne. The possible connexion with cyclical vomiting is discussed. The monograph contains an extensive (though not, as stated by the publisher, a complete) bibliography relating to glycogen disease.

Le Syndrome de Diabète Rénale avec Rachitisme Osteomalacique Incurable et Troubles du Développement chez l'Enfant. By ROBERT DEBRÉ. 1948. Paris: C. Doin et Cie. Pp. 65. (Price 145 *fr.*)

The syndrome, known variously by the names of Fanconi, Toni-Fanconi and Debré-Fanconi, is described in detail, and original observations are added. The possible relationship to a disturbance of cystine metabolism is discussed.

An Introduction to Physical Methods of Treatment in Psychiatry. By W. SARGANT, M.A., M.B., M.R.C.P., D.P.M., Physician, Maudsley Hospital; and E. SLATER, M.A., M.D., F.R.C.P., D.P.M., Physician in Psychological Medicine, National Hospital, Queen Square. Second Edition. 1948. Edinburgh: E. and S. Livingstone Ltd. Pp. 215. (Price 10*s.* 6*d.*)

Although concerned primarily with the treatment of adults, this book will be of value to all who wish to know the physical methods of treatment available in psychiatry, and their indications and limitations. It is concise, clearly written, and based largely on personal experience. In the chapter on epilepsy a short section is devoted to behaviour problem children.

Catalogue of Medical Films. Compiled by the Royal Society of Medicine and the Scientific Film Association. 1948. London: Aslib. Pp. 126. (Price 7*s.* 6*d.*)

This catalogue contains a list of eight hundred titles of medical films and details of two hundred; the first is arranged alphabetically and also subdivided into subject groups. Under Paediatrics, some twenty-five films are listed and details are given of eleven of them (basal narcosis, abdominal sympathectomy, treatment of talipes equino-varus,

achondroplasia, renal infantilism, anterior and posterior plaster beds, two on the Kenny concept and treatment of infantile paralysis, and three on breast feeding, including the treatment of retracted nipples). There are in addition a considerably larger number of films dealing with various aspects of public health and personal hygiene which have a more or less direct paediatric interest. It will be obvious, however, that if the film is to be used extensively in teaching paediatrics, there is ample scope for the production in this country of films dealing either with disease in childhood or with normal development.

The Diagnosis of Threadworm Infestation. (Film strip no. W.16, with lecture notes.) Technical advisers: R. C. MacKeith, D.M., M.R.C.P., D.C.H., and J. M. Watson, D.Sc., A.R.C.S. 1948. London: Unicorn Head, British Industrial Films Ltd. (No price given.)

This film strip, which is available in 18 × 24 mm. or 24 × 36 mm. and as photographic prints (8 × 11 cm and 11·5 × 21·5 cm.), consists of eighteen frames showing first the mature female threadworm emerging from the anus (horrific), and subsequently the detailed technique of collecting ova (a) by the adhesive cellophane tape method and (b) by the glass pestle method (educational). Explanatory lecture notes are provided for each frame, and both illustrations and notes are clear and well chosen.

Since the film-strip projector is easily portable and the film strip itself can be carried in a capacious waistcoat pocket, there are obvious advantages over the lantern in this method of visual teaching. The main disadvantage of the film strip in lecturing is that the sequence of illustrations cannot be altered at will or insertions made. There is, however, a very definite place for film strips of this type dealing with a particular technique, and we wish the Unicorn Head Film Strip Library by which it is issued every success with further productions.